

# SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Sabiha Qazi Examiner #: 74141 Date: 10/28/04  
 Art Unit: 1616 Phone Number: 2020622 Serial Number: 09/939,208  
 Mail Box and Bldg/Room Location: 4C70, Rm, 4A45 Results Format Preferred (circle) PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

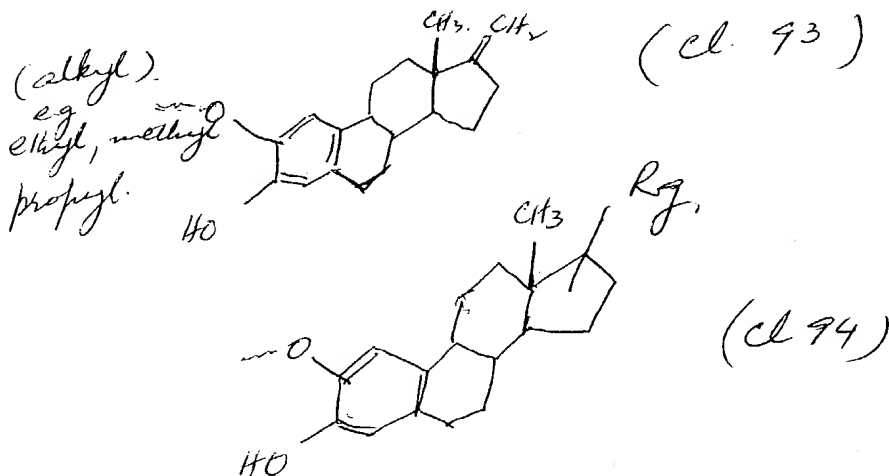
\*\*\*\*\*  
 Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Antianitrogenic Agents

Inventors (please provide full names): Gregory E. Agoston, et al

Earliest Priority Filing Date: 8/24/01

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



Please see attached sheets

Thanks

## STAFF USE ONLY

	Type of Search	Vendors and cost where applicable
Searcher: <u>Qazi</u>	NA Sequence (#) _____	STN <input checked="" type="checkbox"/>
Searcher Phone #: <u>22504</u>	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) <input checked="" type="checkbox"/>	Questel/Orbit _____
Date Searcher Picked Up: <u>10/28</u>	Bibliographic _____	Dr. Link _____
Date Completed: <u>10/28</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: <u>15</u>	Patent Family _____	WWW/Internet _____
Online Time: <u>125</u>	Other _____	Other (specify) _____

=> fil reg

FILE 'REGISTRY' ENTERED AT 14:03:30 ON 28 OCT 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 27 OCT 2004 HIGHEST RN 770693-70-4

DICTIONARY FILE UPDATES: 27 OCT 2004 HIGHEST RN 770693-70-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

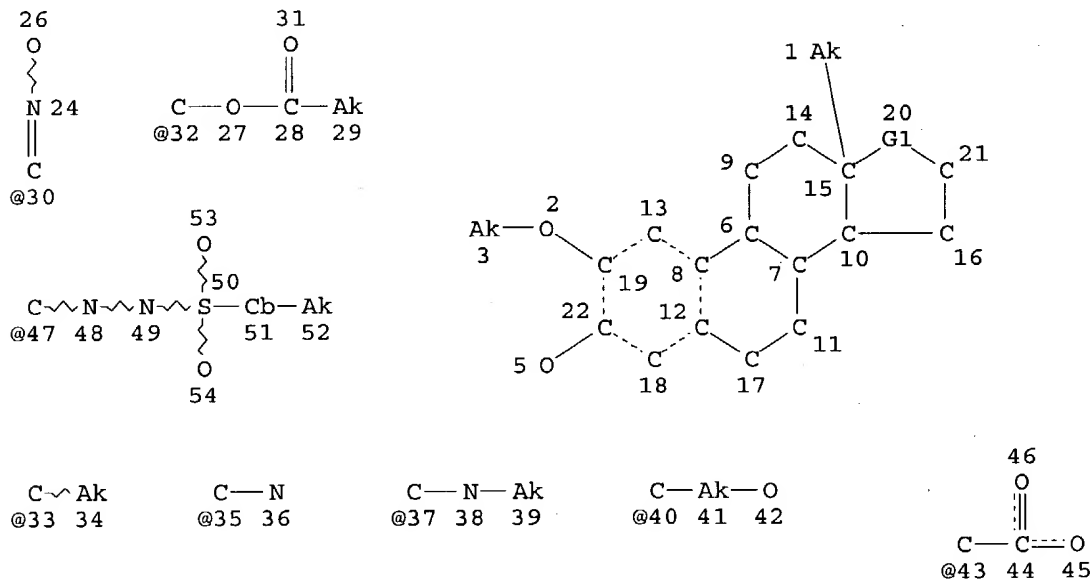
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que l13

L9 STR



VAR G1=33/30/32/37/40/43/47/35

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 15

NUMBER OF NODES IS 51

STEREO ATTRIBUTES: NONE

L12 234 SEA FILE=REGISTRY SSS FUL L9

L13 32 SEA FILE=REGISTRY SUB=L12 CSS FUL L9

100.0% PROCESSED 234 ITERATIONS

32 ANSWERS

SEARCH TIME: 00.00.01

=> d his

(FILE 'HOME' ENTERED AT 13:43:08 ON 28 OCT 2004)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 13:43:14 ON 28 OCT 2004

FILE 'HCAPLUS' ENTERED AT 13:43:29 ON 28 OCT 2004

L1 1 S US20020082433/PN  
SEL RN

FILE 'REGISTRY' ENTERED AT 13:43:37 ON 28 OCT 2004

L2 68 S E1-E68  
L3 63 S L2 AND C5-C6-C6-C6/ES  
L4 19 S L3 AND 2/O  
L5 1 S L4 AND C20H26O2  
E C20H26O2/MF  
L6 146 S E3 AND 4432.3.65/RID  
L7 146 S L6 AND 4/NR  
L8 2 S L7 AND 2 METHOXY  
L9 STR  
L10 0 S L9 CSS SAM  
L11 12 S L9 SAM  
L12 234 S L9 FUL  
SAV TEMP QAZI939/A L12  
L13 32 S L9 CSS FUL SUB=L12  
SAV TEMP L13 QAZI939A/A  
L14 12 S L2 AND L13  
L15 20 S L13 NOT L14  
L16 3 S L15 AND (C21H28O4 OR C21H28O2)

FILE 'HCAOLD' ENTERED AT 13:59:44 ON 28 OCT 2004

L17 0 S L14  
L18 2 S L16  
SEL AN  
EDIT E1-E2 /OR  
EDIT /AN /OREF

FILE 'HCAPLUS' ENTERED AT 14:00:47 ON 28 OCT 2004

L19 3 S E1-E2  
L20 2 S L19 NOT MAZUR ?/AU  
L21 6 S L14  
L22 11 S L16  
L23 15 S L20-L22  
L24 3 S L23 AND (AGOSTON G? OR SHAH J? OR HUNSUCKER K? OR PRIBLUDA V?  
L25 2 S L23 AND ENTREMED?/PA,CS  
L26 3 S L1,L24,L25  
L27 12 S L23 NOT L26

FILE 'USPATFULL, USPAT2' ENTERED AT 14:03:09 ON 28 OCT 2004

L28 4 S L14 OR L16

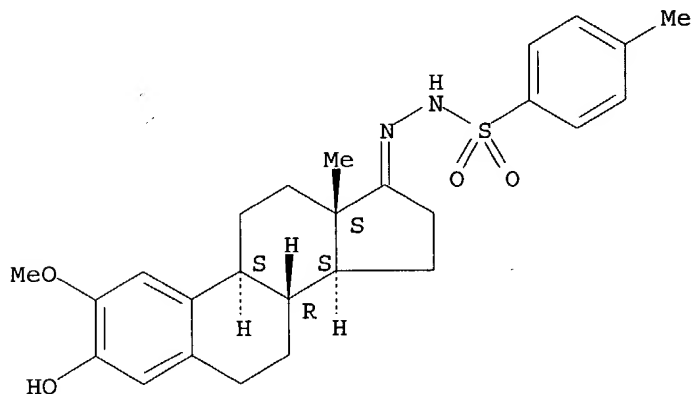
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=> d ide can tot l14

L14 ANSWER 1 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 438044-29-2 REGISTRY  
CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-

17-ylidene)hydrazide (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C26 H32 N2 O4 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
 DT.CA Caplus document type: Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.  
 Double bond geometry unknown.



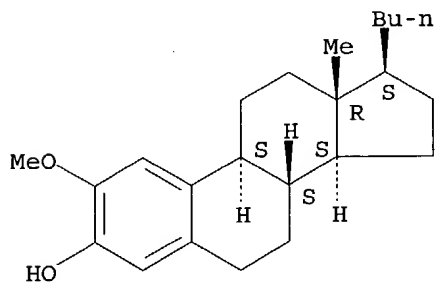
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1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

L14 ANSWER 2 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 431901-78-9 REGISTRY  
 CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C23 H34 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
 DT.CA Caplus document type: Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

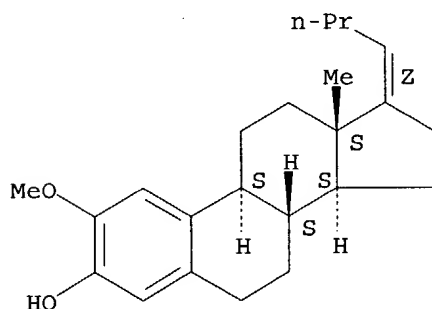
REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 3 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 431901-77-8 REGISTRY  
CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z) - (9CI)  
(CA INDEX NAME)  
FS STEREOSEARCH  
MF C23 H32 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA CAplus document type: Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT  
(Reactant or reagent); USES (Uses)

Absolute stereochemistry.  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

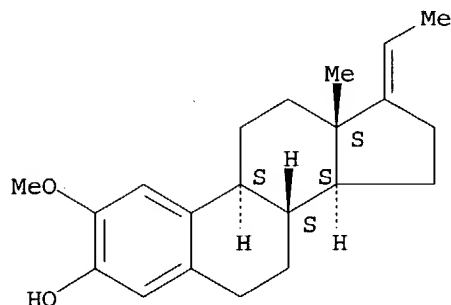
REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 4 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 431901-75-6 REGISTRY  
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX  
NAME)  
FS STEREOSEARCH  
MF C21 H28 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA CAplus document type: Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT  
(Reactant or reagent); USES (Uses)

Absolute stereochemistry.

Double bond geometry unknown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

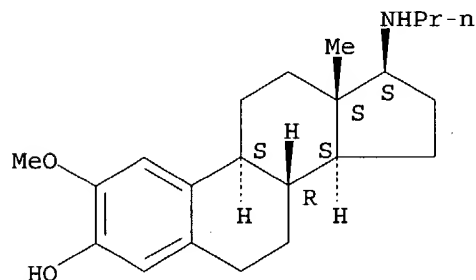
2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

REFERENCE 2: 137:6309

L14 ANSWER 5 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 431901-74-5 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17 $\beta$ )- (9CI)  
(CA INDEX NAME)  
FS STEREOSEARCH  
MF C22 H33 N O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA Caplus document type: Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES  
(Uses)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

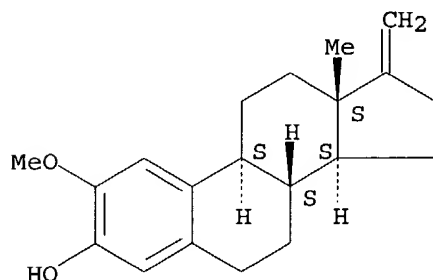
REFERENCE 1: 137:47357

REFERENCE 2: 137:6309

L14 ANSWER 6 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 431901-73-4 REGISTRY

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 2-Methoxy-17(20)-methylenestra-1,3,5(10)-trien-3-ol  
 CN 3-Hydroxy-2-methoxy-17(20)-methylenestra-1,3,5(10)-triene  
 FS STEREOSEARCH  
 MF C20 H26 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
 DT.CA Caplus document type: Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT  
 (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



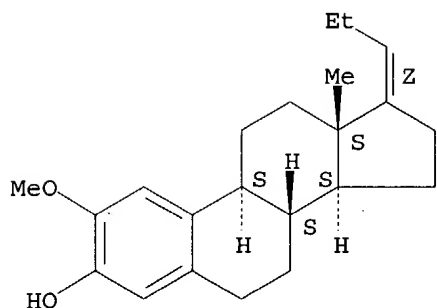
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 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:243723  
 REFERENCE 2: 140:73598  
 REFERENCE 3: 137:47357  
 REFERENCE 4: 137:6309

L14 ANSWER 7 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 431901-72-3 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA  
 INDEX NAME)  
 FS STEREOSEARCH  
 MF C22 H30 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
 DT.CA Caplus document type: Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT  
 (Reactant or reagent); USES (Uses)

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 8 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN

RN 431901-71-2 REGISTRY

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 2-Methoxy-17β-methylestra-1,3,5(10)-trien-3-ol

CN 3-Hydroxy-2-methoxy-17β-methylestra-1,3,5(10)-triene

FS STEREOSEARCH

MF C20 H28 O2

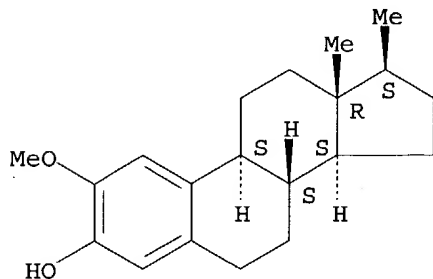
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1907 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:243723



REFERENCE 2: 139:224972

REFERENCE 3: 137:47357

REFERENCE 4: 137:6309

L14 ANSWER 9 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN

RN 431901-70-1 REGISTRY

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C22 H32 O2

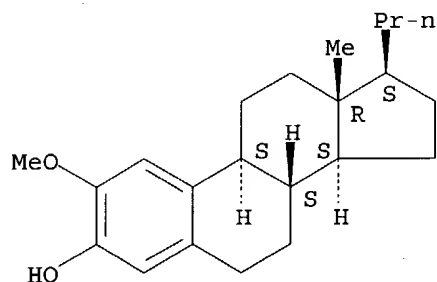
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 10 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN

RN 431901-69-8 REGISTRY

CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C19 H25 N O3

SR CA

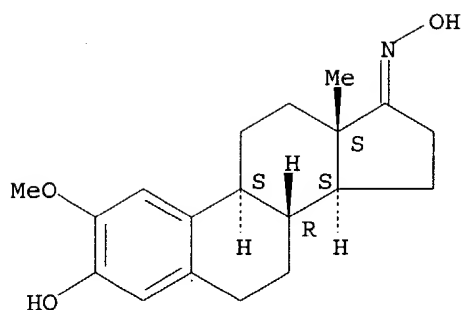
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

Double bond geometry unknown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 11 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN

RN 431901-68-7 REGISTRY

CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17β)- (9CI) (CA  
INDEX NAME)

FS STEREOSEARCH

MF C19 H27 N O2

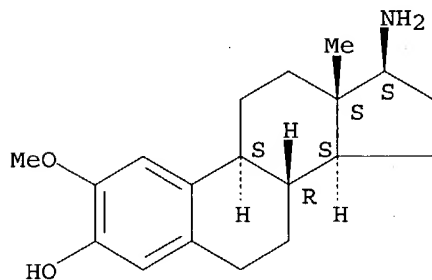
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES  
(Uses)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

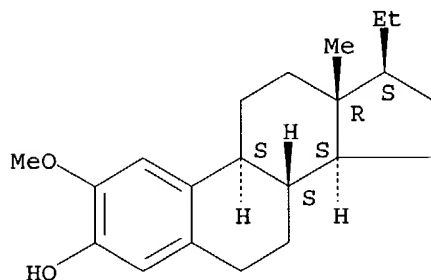
REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 12 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 229486-18-4 REGISTRY  
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C21 H30 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA CAplus document type: Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT  
(Reactant or reagent); USES (Uses)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

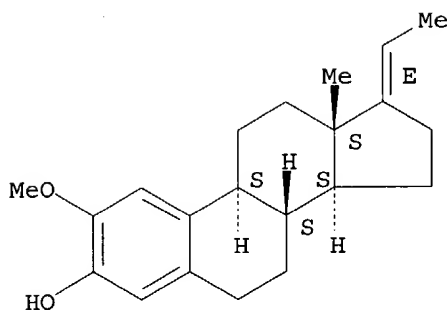
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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972  
REFERENCE 2: 137:47357  
REFERENCE 3: 137:6309  
REFERENCE 4: 131:88083

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L16 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 594873-87-7 REGISTRY  
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17E)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C21 H28 O2  
SR CA  
LC STN Files: CA, CAPLUS  
DT.CA CAplus document type: Patent  
RL.P Roles from patents: PREP (Preparation)

Absolute stereochemistry.  
Double bond geometry as shown.



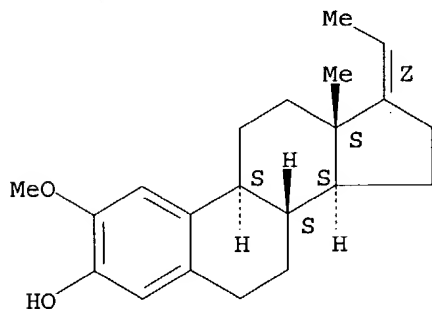
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1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

L16 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 229486-17-3 REGISTRY  
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA  
INDEX NAME)  
FS STEREOSEARCH  
MF C21 H28 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA Caplus document type: Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT  
(Reactant or reagent)

Absolute stereochemistry.  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5 REFERENCES IN FILE CA (1907 TO DATE)  
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:73598

REFERENCE 2: 137:370278

REFERENCE 3: 135:358085

REFERENCE 4: 133:350395

REFERENCE 5: 131:88083

L16 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN

RN 52717-98-3 REGISTRY

CN Estradiol, 17-acetate, (17 $\beta$ )-  
(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Estradiol, 2-methoxy-, 17-acetate (6CI)

FS STEREOSEARCH

MF C21 H28 O4

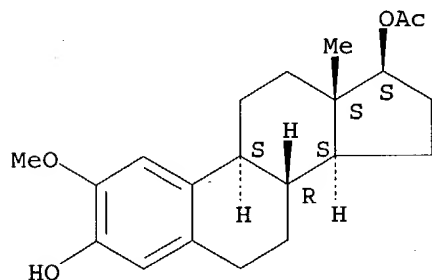
LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, TOXCENTER  
(\*File contains numerically searchable property data)

DT.CA CAPLUS document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT  
(Reactant or reagent); USES (Uses)

RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent);  
NORL (No role in record)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5 REFERENCES IN FILE CA (1907 TO DATE)  
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:369731

REFERENCE 2: 134:295993

REFERENCE 3: 88:121515

REFERENCE 4: 81:4163

REFERENCE 5: 54:97743

=> fil hcaold

FILE 'HCAOLD' ENTERED AT 14:03:52 ON 28 OCT 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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PRE-1967 CHEMICAL ABSTRACTS FILE WITH HOUR-BASED PRICING

FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate  
substance identification. Title keywords, authors, patent

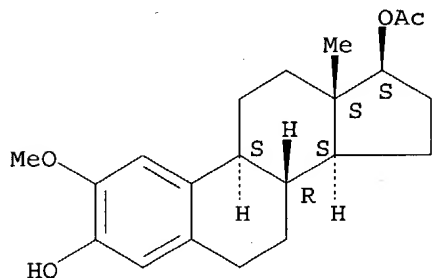
assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d all hitstr tot l18

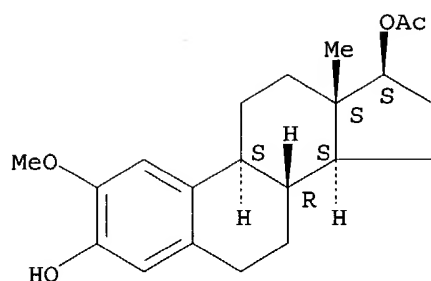
L18 ANSWER 1 OF 2 HCAOLD COPYRIGHT 2004 ACS on STN  
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 TI catechol derivs. of estrogens  
 AU Fishman, Jack; Tomasz, M.; Lehman, R.  
 TI studies using anterior pituitary hormones as antigens  
 AU Fishman, Joseph; McGarry, E. E.; Beck, J. C.  
 IT 1236-72-2 5976-64-7 5976-65-8 5976-67-0 5976-70-5 21696-98-0  
 23463-05-0 28818-82-8 52717-98-3 52717-99-4 59495-33-9  
 116282-36-1 117921-01-4 121176-83-8 121212-59-7 121212-60-0 122426-55-5  
 IT 52717-98-3  
 RN 52717-98-3 HCAOLD  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17 $\beta$ )-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 2 OF 2 HCAOLD COPYRIGHT 2004 ACS on STN  
 AN CA52:13765i CAOLD  
 TI synthesis of 2-methoxyestrogens  
 AU Fishman, Jack  
 IT 362-07-2 362-08-3 7291-57-8 38781-50-9 52717-98-3  
 65932-49-2 65932-50-5 65932-51-6 65932-52-7 65932-53-8 84509-93-3  
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 RN 52717-98-3 HCAOLD  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17 $\beta$ )-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 14:05:22 ON 28 OCT 2004

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FILE COVERS 1907 - 28 Oct 2004 VOL 141 ISS 18

FILE LAST UPDATED: 27 Oct 2004 (20041027/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 130

L30 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1960:97743 HCAPLUS

DN 54:97743

OREF 54:18587e-i,18588a-e

ED Entered STN: 22 Apr 2001

TI Catechol derivatives of estrogens

AU Fishman, Jack; Tomasz, Maria; Lehman, Rosemarie

CS Sloan-Kettering Inst. for Cancer Research, New York, NY

SO Journal of Organic Chemistry (1960), 25, 585-8

CODEN: JOCEAH; ISSN: 0022-3263

DT Journal

LA Unavailable

CC 10J (Organic Chemistry: Steroids)

OS CASREACT 54:97743

AB Preps. of 2-methoxyestriol (I), 2-hydroxyestriol (II) 3-Me ether (III), 2-hydroxyestradiol (IV) 3-Me ether (V), 2-methoxyestrone 3-Me ether (VI), and 2-hydroxyestrone (VII), with various derivs. and intermediates were described. Estriol (8.3 g.) in 250 ml. 95% alc. containing 1.5 g. KOH refluxed 48 hrs. with 6.5 g. 2-chloro-5-nitrobenzophenone, acidified to pH 3, extracted continuously 24 hrs. with Et2O, the extract evaporated and the product

chromatographed on Al2O3 gave 5.6 g. crude material and 1.5 g. unchanged estriol. The product on recrystn. gave 16 $\alpha$ ,17 $\beta$ -dihydroxy-

[ $\alpha$ ]<sub>D</sub> 28D 89°. XIII (240 mg.) in 20 cc. piperidine refluxed 1 hr., cooled, diluted with 100 cc. C<sub>6</sub>H<sub>6</sub>, washed with dilute H<sub>2</sub>SO<sub>4</sub>, dried, evaporated, the residual oil subjected to a 99-transfer countercurrent distribution between 70% aqueous MeOH and CCl<sub>4</sub>, and the combined tubes 14-32 filtered through Al<sub>2</sub>O<sub>3</sub> and crystallized from aqueous MeOH gave 108 mg. 2-methoxyestrone, blades, m. 188-91°, giving with NaOH and BzCl the 3-monobenzoate, needles, m. 225-8°, which was also obtained by oxidation of XI with CrO<sub>3</sub>.

- IT Estra-1,3,5(10)-trien-17 $\beta$ -ol, 3-(2-benzoyl-4-nitrophenoxy)-  
Estra-1,3,5(10)-trien-17 $\beta$ -ol, 3-(2-benzoyl-4-nitrophenoxy)-, acetate  
Estra-1,3,5(10)-trien-17 $\beta$ -ol, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy-  
Estra-1,3,5(10)-trien-17 $\beta$ -ol, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy-  
, acetate  
IT 362-07-2, Estradiol, 2-methoxy-  
(and derivs.)  
IT 362-08-3, Estrone, 2-methoxy- 38781-50-9, Benzophenone,  
2-(2,17 $\beta$ -dihydroxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro-, 17-acetate  
65932-49-2, Benzophenone, 2-(17 $\beta$ -hydroxyestra-1,3,5(10)-trien-3-  
yloxy)-5-nitro- 65932-50-5, Benzophenone, 2-(17 $\beta$ -hydroxyestra-  
1,3,5(10)-trien-3-yloxy)-5-nitro-, acetate 65932-51-6, Benzophenone,  
2-(17 $\beta$ -hydroxy-2-methoxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro-,  
acetate 65932-52-7, Benzophenone, 2-(17 $\beta$ -hydroxy-2-methoxyestra-  
1,3,5(10)-trien-3-yloxy)-5-nitro- 65932-53-8, Estra-1,3,5(10)-trien-17-  
one, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy- 103278-44-0,  
Estra-1,3,5(10)-trien-17-one, 3-(2-benzoyl-4-nitrophenoxy)- 120024-00-2,  
Estrone, 2-methoxy-, benzoate  
(preparation of)

=> s 127 not 130

L31 10 L27 NOT L30

=> d all hitstr tot

L31 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2004:718556 HCAPLUS  
DN 141:243723  
ED Entered STN: 02 Sep 2004  
TI Preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an  
antitumor action  
IN Hillisch, Alexander; Peters, Olaf; Gege, Christian; Regenhardt, Wilko;  
Kosemund, Dirk; Siemeister, Gerhard; Unger, Eberhard; Bothe, Ulrich  
PA Schering Aktiengesellschaft, Germany  
SO PCT Int. Appl., 47 pp.  
CODEN: PIXXD2  
DT Patent  
LA German  
IC ICM C07J041-00  
ICS A61K031-565; A61P035-00  
CC 32-3 (Steroids)  
Section cross-reference(s): 1, 2, 63  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004074307	A1	20040902	WO 2004-EP1606	20040219
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,				



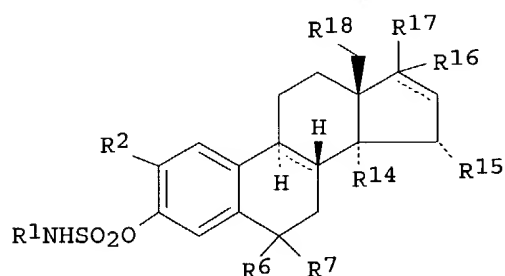
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,  
MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG

DE 10307104 A1 20040923 DE 2003-10307104 20030219  
PRAI DE 2003-10307104 A 20030219

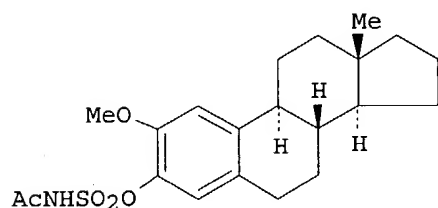
## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004074307	ICM	C07J041-00
	ICS	A61K031-565; A61P035-00

GI



I



II

AB The invention relates to the use of 2-substituted estro-1,3,5(10)-trien-3-yl sulfamates I [R1 = H, C1-5-alkyl, C1-5-acyl; R2 = C1-5-alkoxy, C1-5-alkyl, O-CnFmHo, with the proviso that if R2 = alkyl, then R17 = C1-5-alkoxy; n = 1 - 6, m > 1, m + o = 2n + 1; R6 = H; R7 = H, OH, NH2, NH-acyl (with the proviso, that when R6 ≠ H and R7 ≠ H, then R17 = C1-5-alkoxy); R6R7 = O, NOH, NO-(C1-5-alkyl); R14, R15 = H; R14R15 = CH2, bond; R16 = H, F, C1-5-alkyl, R17 = H, F, C1-5-alkoxy (with the proviso that when R16 = H, R17 = CHXY where X = H, F, C1-4-alkyl; Y = H, F; if X = F, then Y = H, F; if X = OH, then Y = H; XY = O; if R16 = F, then R17 = H or F); R16R17 = :CAB; A, B = H, F, C1-5-alkyl; R18 = H, Me (with the proviso that when R18 = Me, then R17 = SO3NHR1); dashed line = single or double bond], in addition to their pharmaceutically acceptable salts for producing a medicament. Thus, 2-methoxyestra-1,3,5(10)-trien-3-yl N-acetylsulfamate (II) was prepared from 2-methoxyestra-1,3,5(10)-trien-3-ol via sulfamoylation with ClSO2NH2 in CH2Cl2 containing 2,6-di(tert-butyl)pyridine followed by acetylation with acetic anhydride. Said compds. have an antitumor action [for N-desacetyl II; IC50 = 0.67 μM for inhibition of tubulin polymerization; IC50 = 0.4 μM vs. NCI-H460 (lung carcinoma ATCC HTB-177); IC50 = 0.4 μM vs. HCT116 (colon cancer ATCC

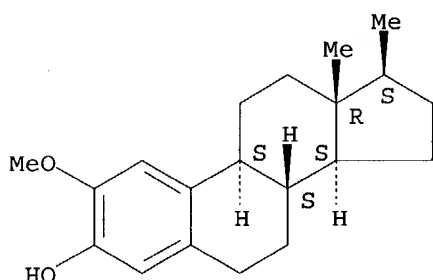
- CCL-247); IC50 = 0.5  $\mu$ M vs. DU145 (prostate cancer ATCC HTB-81); IC50 = 0.11  $\mu$ M vs. MaTu/ADT (breast cancer Epo GmbH Berlin); IC50 = <0.1  $\mu$ M vs. HMVEC (endothelial cells)] .
- ST estratrienyl sulfamate deriv prepn antitumor tubulin polymn inhibitor;  
breast cancer inhibitor estratrienyl sulfamate deriv prepn
- IT Endothelium  
(antiproliferants; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl  
sulfamates with an antitumor action)
- IT Mammary gland, neoplasm  
Prostate gland, neoplasm  
(carcinoma, medicinals; preparation of 2-substituted  
estra-1,3,5(10)-trien-3-  
yl sulfamates with an antitumor action)
- IT Intestine, neoplasm  
(colon, medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl  
sulfamates with an antitumor action)
- IT Cell proliferation  
(inhibition; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl  
sulfamates with an antitumor action)
- IT Lung, neoplasm  
Mammary gland, neoplasm  
Reproductive organ, neoplasm  
(medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl  
sulfamates with an antitumor action)
- IT Tubulins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(polymerization, inhibition; preparation of 2-substituted  
estra-1,3,5(10)-trien-3-  
yl sulfamates with an antitumor action)
- IT Antitumor agents  
Cytotoxic agents  
Human  
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an  
antitumor action)
- IT Estrogens  
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);  
USES (Uses)  
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an  
antitumor action)
- IT 362-08-3, 3-Hydroxy-2-methoxyestra-1,3,5(10)-trien-17-one  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(Wittig methylenation or Grignard reaction of, with allylmagnesium  
bromide; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates  
with an antitumor action)
- IT 752246-14-3, 3-Acetoxy-2-methoxy-18a-homoestra-1,3,5(10)-triene  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(benzylic oxidation of, with chromium trioxide; preparation of 2-substituted  
estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 752246-09-6, 3-Acetoxy-2-methoxy-17(20)-methylene-6-oxoestra-1,3,5(10)-  
triene  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(deacetylation and sulfamoylation of; preparation of 2-substituted  
estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 185910-34-3, 2-Methoxy-17-oxoestra-1,3,5(10)-trien-3-yl sulfamate  
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT  
(Reactant or reagent); USES (Uses)  
(oximation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl  
sulfamates with an antitumor action)
- IT 208924-88-3DP, Estra-1,3,5(10)-triene-3-yl sulfamate, derivs.  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and acylation of, with anhydrides; preparation of 2-substituted

- estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 752246-13-2P, 17 $\alpha$ -(Azidomethyl)-3,17 $\beta$ -dihydroxy-2-methoxyestra-1,3,5(10)-triene  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and azide reduction of; preparation of 2-substituted  
 estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 752245-83-3P, 2-Methoxy-17(20)-methylene-6-oxoestra-1,3,5(10)-trien-3-yl sulfamate  
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation and benzylic oxidation of, with chromium oxide; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 752246-07-4P, 2-(1-Methoxyethyl)-3-(benzyloxy)-17 $\beta$ -methoxyestra-1,3,5(10)-triene  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and hydrogenolysis of; preparation of 2-substituted  
 estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 752245-92-4P, 2-Methoxy-6-oxo-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate  
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation and reduction or oximation of; preparation of 2-substituted  
 estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 748807-33-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reduction or sulfamoylation of; preparation of  
 2-substituted  
 estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 752246-12-1P, 3-Hydroxy-2-methoxyestra-1,3,5(10)-triene-17 $\beta$ -spiro-1',2'-oxiran  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and regioselective azidation of; preparation of 2-substituted  
 estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 752246-06-3P, 17 $\alpha$ -Allyl-2-methoxyestra-1,3,5(10)-trien-3,17 $\beta$ -diol  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and sulfamoylation of, with sulfamoyl chloride; preparation of  
 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor  
 action)
- IT 431901-71-2P, 3-Hydroxy-2-methoxy-17 $\beta$ -methylestra-1,3,5(10)-triene 752246-08-5P, 2-Ethyl-3-hydroxy-17 $\beta$ -methoxyestra-1,3,5(10)-triene 752246-11-0P, 17 $\beta$ -Difluoromethyl-3-hydroxy-2-methoxyestra-1,3,5(10)-triene 752246-15-4P, 17 $\alpha$ -Fluoro-3-hydroxy-2-methoxyestra-1,3,5(10)-triene  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and sulfamoylation of; preparation of 2-substituted  
 estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 431901-73-4P, 3-Hydroxy-2-methoxy-17(20)-methyleneestra-1,3,5(10)-triene 752246-10-9P, 17(20)-Difluoromethylene-3-hydroxy-2-methoxyestra-1,3,5(10)-triene  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and sulfamoylation or stereoselective hydrogenation of;  
 preparation  
 of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an

- antitumor action)  
IT 33069-62-4, Taxol  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 748807-30-9P 748807-31-0P 748807-32-1P 752245-75-3P,  
2-Methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-76-4P,  
2-Methoxyestra-1,3,5(10)-trien-3-yl N-acetylsulfamate 752245-77-5P,  
2-Methoxy-6-(oximino)estra-1,3,5(10)-trien-3-yl sulfamate 752245-78-6P,  
2-Methoxyestra-1,3,5(10),16-tetraen-3-yl sulfamate 752245-79-7P,  
2-Methoxy-17-[(E)-vinylmethylenestra-1,3,5(10)-trien-3-yl sulfamate  
752245-80-0P, 2-Ethyl-17 $\beta$ -methoxyestra-1,3,5(10)-trien-3-yl sulfamate  
752245-81-1P, 2-Methoxy-17(20)-methylenestra-1,3,5(10)-trien-3-yl  
sulfamate 752245-82-2P, 2-Methoxy-17 $\beta$ -methylestra-1,3,5(10)-trien-3-  
yl sulfamate 752245-84-4P, 2-Methoxy-17(20)-methylene-6-oximinoestra-  
1,3,5(10)-trien-3-yl sulfamate 752245-85-5P, 17(20)-Difluoromethylene-2-  
methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-86-6P,  
17 $\beta$ -Difluoromethyl-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate  
752245-87-7P, 2-Methoxyestra-1,3,5(10),14-tetraen-3-yl sulfamate  
752245-88-8P, 17,17-Difluoro-2-methoxyestra-1,3,5(10),14-tetraen-3-yl  
sulfamate 752245-89-9P, 17,17-Difluoro-2-methoxy-18a-homoestra-  
1,3,5(10),14-tetraen-3-yl sulfamate 752245-90-2P, 17 $\beta$ -Formyl-2-  
Methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-91-3P,  
17 $\beta$ -Hydroxymethyl-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate  
752245-93-5P, 2-Methoxy-6-oximino-18a-homoestra-1,3,5(10)-trien-3-yl  
sulfamate 752245-94-6P, 2-Methoxy-6-(O-methyloximino)-18a-homoestra-  
1,3,5(10)-trien-3-yl sulfamate 752245-95-7P, 6 $\alpha$ -Acetylamino-2-  
methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-96-8P,  
6 $\alpha$ -Hydroxy-2-methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate  
752245-97-9P, 17 $\alpha$ -Fluoro-2-methoxyestra-1,3,5(10)-trien-3-yl  
sulfamate 752245-98-0P, 17 $\beta$ -Fluoro-2-methoxyestra-1,3,5(10)-trien-3-  
yl sulfamate 752245-99-1P, 17,17-Difluoro-2-methoxyestra-1,3,5(10)-trien-  
3-yl sulfamate 752246-00-7P, 17,17-Difluoro-2-methoxy-6-oximinoestra-  
1,3,5(10)-trien-3-yl sulfamate 752246-01-8P, 17,17-Difluoro-2-methoxy-  
18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752246-02-9P,  
17,17-Difluoro-2-methoxy-6-oximino-18a-homoestra-1,3,5(10)-trien-3-yl  
sulfamate 752246-03-0P, 17,17-Difluoro-2-methoxyestra-1,3,5(10)-trien-3-  
yl N-acetylsulfamate 752246-04-1P, 2-Methoxy-17-[(E)-oximino]estra-  
1,3,5(10)-trien-3-yl sulfamate 752246-05-2P, 17 $\alpha$ -Allyl-17 $\beta$ -  
hydroxy-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an  
antitumor action)
- IT 362-07-2, 2-Methoxyestra-1,3,5(10)-triene-3,17 $\beta$ -diol  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(regioselective fluorination of, with DAST; preparation of 2-substituted  
estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 26357-04-0, 2-Acetyl-3-(benzyloxy)estra-1,3,5(10)-trien-17-one  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(stereoselective reduction and O-methylation of; preparation of  
2-substituted  
estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- IT 1217-09-0D, Estra-1,3,5(10)-triene, derivs. 4953-96-2,  
2-Methoxyestra-1,3,5(10)-trien-3-ol  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(sulfamoylation of, with sulfamoyl chloride; preparation of 2-substituted  
estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
- RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE  
(1) Ina, S; WO 0118028 A 2001  
(2) Maccarthy-Morrogh, L; CANCER RESEARCH 2000, V60(19), P5441 HCAPLUS

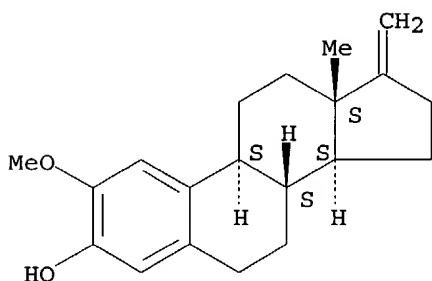
(3) Purohit, A; JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY 1999, V69(1/6), P227  
 (4) Singh, A; MOLECULAR AND CELLULAR ENDOCRINOLOGY 2000, V160, P61 HCAPLUS  
 (5) Stanford Res Inst Int; WO 9933858 A 1999 HCAPLUS  
 IT **431901-71-2P**, 3-Hydroxy-2-methoxy-17 $\beta$ -methylestra-1,3,5(10)-triene  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and sulfamoylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)  
 RN 431901-71-2 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **431901-73-4P**, 3-Hydroxy-2-methoxy-17(20)-methylenestra-1,3,5(10)-triene  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and sulfamoylation or stereoselective hydrogenation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)  
 RN 431901-73-4 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2004:3558 HCAPLUS  
 DN 140:73598  
 ED Entered STN: 04 Jan 2004  
 TI Systems and methods for rapid evaluation and design of molecules for predicted biological activity  
 IN Hendry, Lawrence B.  
 PA USA  
 SO U.S. Pat. Appl. Publ., 44 pp.

CODEN: USXXCO

DT Patent

LA English

IC ICM A01N001-00

NCL 435001100

CC 9-16 (Biochemical Methods)

Section cross-reference(s): 1, 3

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004002052	A1	20040101	US 2002-279546	20021023
PRAI	US 2001-344560P	P	20011023		
	US 2001-339954P	P	20011210		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004002052	ICM	A01N001-00
	NCL	435001100

AB The computer-based systems and methods are for rapidly evaluating mols. for suspected biol. activity and relative potency, and for designing mols. for desired biol. activity. The systems and methods enable rapid screening of large mol. databases using one or more search engines designed to identify mols. predicted to possess specific biol. activities. Estradiol, 8 other estrogens and the conformation of the DNA site into which they fit were used to construct a search engine which was used to search databases containing a variety of compound structures.

ST system rapid evaluation design mol predicted biol activity; computer system design evaluation biol activity; large mol database search engine biol activity; estrogen search engine screening

IT Named reagents and solutions  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Horeau's acid, identified by estrogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Antibiotics  
(against anthrax, evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Bacillus anthracis  
(anthrax from, antibiotics against, evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Electrostatic potential  
(between mol. and binding site, in creating search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Nucleic acids  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(creating search engines for mols. binding specified sites in; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Penis  
(erectile activity, evaluation of substances for; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Angiogenesis inhibitors  
Antidepressants  
Antidiabetic agents  
Carcinogens  
Hypnotics and Sedatives  
Selective estrogen receptor modulators  
(evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

- activity)
- IT Androgens  
Estrogens  
Glucocorticoids  
Progestogens  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(evaluation of substances for predicted activity of; systems and  
methods for rapid evaluation and design of mols. for predicted biol.  
activity)
- IT Bone  
Thyroid gland  
(evaluation of substances for predicted activity on; systems and  
methods for rapid evaluation and design of mols. for predicted biol.  
activity)
- IT Sexual behavior  
(impotence, evaluation of substances for predicted erectile activity  
and treatment of; systems and methods for rapid evaluation and design  
of mols. for predicted biol. activity)
- IT Databases  
(large mol., systems and methods and search engines for rapid screening  
of; systems and methods for rapid evaluation and design of mols. for  
predicted biol. activity)
- IT Information systems  
(network; systems and methods for rapid evaluation and design of mols.  
for predicted biol. activity)
- IT Information systems  
(searching; systems and methods for rapid evaluation and design of  
mols. for predicted biol. activity)
- IT Apparatus  
Bioinformatics  
Computer program  
Computers  
Conformation  
Data processing  
Design  
Drug design  
Excluded volume  
Functional groups  
Hydrogen bond  
Molecular shape  
Molecular surface  
Molecules  
Simulation and Modeling, biological  
Simulation and Modeling, physicochemical  
Structure-activity relationship  
Volume  
(systems and methods for rapid evaluation and design of mols. for  
predicted biol. activity)
- IT DNA  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(systems and methods for rapid evaluation and design of mols. for  
predicted biol. activity)
- IT 388075-75-0, PDC 7  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(PDC 7, identified by estrogenic search engine; systems and methods for  
rapid evaluation and design of mols. for predicted biol. activity)
- IT 58-22-0, Testosterone 434-22-0, 19-Nortestosterone 521-11-9,  
17 $\alpha$ -Methyl-5 $\alpha$ -dihydrotestosterone 521-18-6, 5 $\alpha$ -  
Dihydrotestosterone 1434-85-1, 5 $\alpha$ -Dihydro-19-nortestosterone  
3704-07-2, 7 $\alpha$ -Methyl-5 $\alpha$ -dihydrotestosterone 3704-08-3  
3764-87-2, 7 $\alpha$ -Methyl-19-nortestosterone 6424-04-0 7642-58-2,

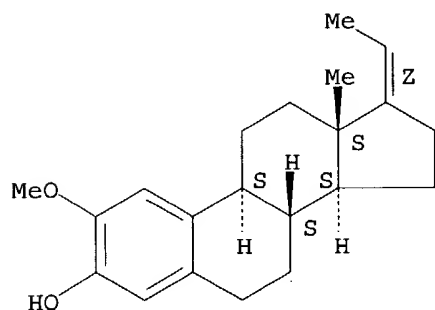
- 7 $\alpha$ -Methyltestosterone 31025-34-0  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as standard in construction of search engine for evaluation of substances  
for predicted androgenic activity; systems and methods for rapid  
evaluation and design of mols. for predicted biol. activity)
- IT 389-08-2, Nalidixic acid 70458-92-3, Pefloxacin 70458-96-7,  
Norfloxacin 79660-72-3, Fleroxacin 85721-33-1, Ciprofloxacin  
98079-51-7, Lomefloxacin 100986-85-4, Levofloxacin 110871-86-8,  
Sparfloxacin 112811-59-3, Gatifloxacin 147059-72-1, Trovafloxacin  
151096-09-2, Moxifloxacin  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as standard in construction of search engine for evaluation of substances  
for predicted anthrax antibiotic activity; systems and methods for  
rapid evaluation and design of mols. for predicted biol. activity)
- IT 362-07-2, 2-Methoxyestradiol 165619-07-8, 2-Ethoxyestradiol  
192062-02-5 229486-17-3 431901-73-4 431901-98-3  
431902-09-9  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as standard in construction of search engine for evaluation of substances  
for predicted antiangiogenic activity; systems and methods for rapid  
evaluation and design of mols. for predicted biol. activity)
- IT 50-48-6, Amitriptyline 50-49-7, Imipramine 303-49-1 5560-72-5,  
Iprindole 10262-69-8, Maprotiline 24526-64-5, Nomifensin 54910-89-3,  
Fluoxetine 79617-96-2, Sertraline  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as standard in construction of search engine for evaluation of substances  
for predicted antidepressant activity; systems and methods for rapid  
evaluation and design of mols. for predicted biol. activity)
- IT 50-28-2, Estradiol, biological studies 57-63-6, 17 $\alpha$ -  
Ethinylestradiol 4567-67-3, 17 $\alpha$ -Chloroethinylestradiol  
21507-14-2, 11 $\beta$ -Methoxyestradiol 34816-55-2, Moxestrol 95258-49-4  
95258-51-8 108887-25-8 130929-98-5 164580-56-7  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as standard in construction of search engine for evaluation of substances  
for predicted estrogenic activity; systems and methods for rapid  
evaluation and design of mols. for predicted biol. activity)
- IT 50-23-7, Cortisol  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as standard in construction of search engine for evaluation of substances  
for predicted glucocorticoid activity; systems and methods for rapid  
evaluation and design of mols. for predicted biol. activity)
- IT 53-43-0, Dehydroepiandrosterone  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as standard in construction of search engine for evaluation of substances  
for predicted penile erectile and anti-impotence activity; systems and  
methods for rapid evaluation and design of mols. for predicted biol.  
activity)
- IT 516-54-1, 3 $\alpha$ , 5 $\alpha$ -Tetrahydroprogesterone 516-55-2  
23930-19-0, Alphaxalone 38398-32-2, Ganaxolone  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as standard in construction of search engine for evaluation of substances  
for predicted sedative activity; systems and methods for rapid  
evaluation and design of mols. for predicted biol. activity)
- IT 15178-66-2  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(dbl. stranded, as DNA binding site used in evaluation of substances  
for predicted anthrax antibiotic activity; systems and methods for  
rapid evaluation and design of mols. for predicted biol. activity)
- IT 4251-20-1  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(dbl. stranded, as DNA binding site used in evaluation of substances



for predicted estrogenic or androgenic or other activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

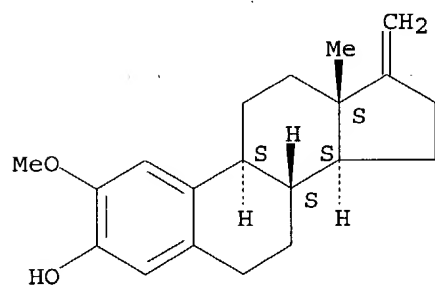
- IT 3704-09-4, Mibolerone  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by androgen search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 69-53-4, Ampicillin 28657-80-9, Cinoxacin  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by anthrax antibiotic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 54-32-0, Moxisylyte 56-87-1, Lysine, biological studies 74-79-3, Arginine, biological studies 497-76-7, Arbutin 2530-97-4, Xanthinol 7665-99-8, Cyclic GMP  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by anti-impotence search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 117-39-5, Quercetin 501-36-0, Resveratrol 26581-81-7, EM-12  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by antiangiogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 17692-37-4, Fantridone 34911-55-2, Bupropion 54739-18-3, Fluvoxamine 71620-89-8, Reboxetine 93413-69-5, Venlafaxine  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by antidepressant search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 124-87-8, Picrotoxin 5938-11-4, Callicarpone 20071-51-6, Eupatoroxin  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by carcinogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 24643-97-8, Indenestrol  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by estrogen search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 56-53-1, trans-Diethylstilbestrol 446-72-0, Genistein 486-66-8, Daidzein 531-95-3, Equol 26538-44-3, Zearalanol  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by estrogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 50-35-1, Thalidomide  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by sedative and antidepressant and antiangiogenic search engines; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 21715-46-8, Etifoxine 61869-08-7, Paroxetine  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by sedative and antidepressant search engines; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 57-43-2, Amobarbital 58-61-7, Adenosine, biological studies 73-31-4, Melatonin 77-26-9, Butalbital 1972-08-3, 89 Tetrahydrocannabinol 20007-85-6, Cyclophenol 57801-81-7, Brotizolam  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (identified by sedative search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- IT 229486-17-3 431901-73-4  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (as standard in construction of search engine for evaluation of substances for predicted antiangiogenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
- RN 229486-17-3 HCAPLUS  
 CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 431901-73-4 HCAPLUS  
CN Estradiol-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:892536 HCAPLUS  
DN 139:369731  
ED Entered STN: 14 Nov 2003  
TI Sustained-release compositions of estradiol metabolites and their derivatives  
IN Allison, Dean S.; Schmidt, Paul G.; Hudnut, Paul S.  
PA PR Pharmaceuticals, Inc., USA  
SO PCT Int. Appl., 35 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM A61K  
CC 63-6 (Pharmaceuticals)  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003092585	A2	20031113	WO 2003-US12727	20030425
	WO 2003092585	A3	20040819		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,				

NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
 GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-377490P P 20020502

## CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

WO 2003092585 ICM A61K

AB The present invention provides improved sustained-release formulations of estradiol metabolites, including 2-hydroxyestradiol, 2-methoxyestradiol, 4-hydroxyestradiol and 4-methoxyestradiol, useful for therapeutic treatments. The invention also provides methods of producing sustained-release forms of estradiol metabolites. The compns. of the present invention include microparticles, nanoparticles, patches, crystals, gels, rods, stints, pellets, disks, lozenges, wafers, capsules, films, microcapsules, nanocapsules, hydrogels, liposomes, implants and vaginal rings. Compns. also include formulations for transdermal and i.v. delivery of estradiol metabolites. The present invention provides numerous improvements over previous forms of estradiol metabolites, such advantages including the sustained release of normally short half-life compds. to maintain therapeutic blood levels. For example, 2-methoxyestradiol transdermal patch was prepared by suspending the drug in pressure-sensitive adhesives and coated onto polyethylene and aluminum vapor coated polyester backings.

ST estradiol metabolite deriv controlled release

IT Drug delivery systems

(capsules; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyoxyalkylenes, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(copolymer with orthoesters and urethanes; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems

(films; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems

(gels; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyesters, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glycolide-based; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems

(hydrogels; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems

(implants; sustained release compns. of estradiol metabolites and their derivs.)

IT Surfactants

(ionic; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyesters, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(lactide; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems

(liposomes; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems

(microcapsules; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems

(microparticles; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems  
(microspheres; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems  
(nanocapsules; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems  
(nanoparticles; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems  
(nasal; sustained release compns. of estradiol metabolites and their derivs.)

IT Surfactants  
(nonionic; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems  
(ophthalmic; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems  
(oral; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyethers, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ortho ester group-containing; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems  
(pellets; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyamides, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(poly(amino acids); sustained release compns. of estradiol metabolites and their derivs.)

IT Polyesters, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyamide-; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyamides, biological studies  
Polyethers, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyester-; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyesters, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyether-; sustained release compns. of estradiol metabolites and their derivs.)

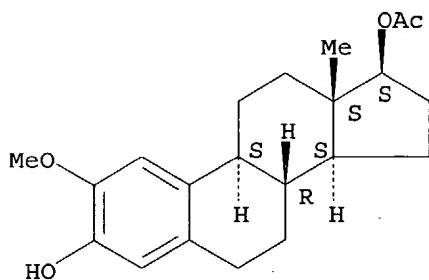
IT Drug delivery systems  
(prodrugs; sustained release compns. of estradiol metabolites and their derivs.)

IT Antioxidants  
Buffers  
Encapsulation  
(sustained release compns. of estradiol metabolites and their derivs.)

IT Lecithins  
Peptides, biological studies  
Phospholipids, biological studies  
Polyanhydrides  
Polycarbonates, biological studies  
Polymer blends  
Polyoxyalkylenes, biological studies  
Polyurethanes, biological studies  
Tocopherols  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sustained release compns. of estradiol metabolites and their derivs.)

- IT Drug delivery systems  
(sustained-release; sustained release compns. of estradiol metabolites and their derivs.)
- IT Drug delivery systems  
(tapes, buccal; sustained release compns. of estradiol metabolites and their derivs.)
- IT Drug delivery systems  
(transdermal; sustained release compns. of estradiol metabolites and their derivs.)
- IT Drug delivery systems  
(vaginal; sustained release compns. of estradiol metabolites and their derivs.)
- IT 106392-12-5  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Poloxamer; sustained release compns. of estradiol metabolites and their derivs.)
- IT 50-28-2D, Estradiol, metabolite, derivs. 121-79-9, Propyl gallate 128-37-0, Butylated hydroxytoluene, biological studies 137-66-6, Ascorbyl palmitate 362-05-0, 2-Hydroxyestradiol 362-07-2, 2-Methoxyestradiol 5976-61-4, 4-Hydroxyestradiol 7002-78-0 7291-56-7 7291-57-8 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinyl pyrrolidone 15802-18-3D, Cyanoacrylic acid, esters, polymers 23463-05-0 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 25322-68-3, Poly(ethylene glycol) 25322-68-3D, Polyethylene glycol, copolymer with orthoesters and urethanes 25322-69-4, Poly(Propylene glycol) 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 26780-50-7, Poly(lactide-co-glycolide) 26780-50-7D, Poly(lactide-co-glycolide), derivs. 26788-23-8, 4-Methoxyestradiol 31621-87-1, Poly(dioxanone) 34346-01-5, Poly(glycolic acid-lactic acid) 37492-86-7 **52717-98-3** 79787-03-4 79795-26-9 83187-96-6 83274-89-9 84509-93-3 111162-54-0 111162-55-1 111162-82-4 144082-85-9 144082-86-0 622839-99-0 622840-00-0 622840-01-1 622840-02-2 622840-03-3 622840-04-4 622840-05-5 622840-06-6 622840-07-7 622840-08-8 622840-09-9 622840-10-2 622840-11-3 622840-12-4 622840-13-5 622840-14-6 622840-15-7 622840-16-8 622840-17-9 622840-32-8  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sustained release compns. of estradiol metabolites and their derivs.)
- IT **52717-98-3**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sustained release compns. of estradiol metabolites and their derivs.)
- RN 52717-98-3 HCAPLUS
- CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17 $\beta$ )-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



DN 137:370278  
 ED Entered STN: 22 Nov 2002  
 TI Preparation of substituted pregna-1,3,5(10)-triene derivatives for pharmaceutical use  
 IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Pechet, Maurice Murdoch; Gile, Michael  
 PA Marsden, John Christopher, UK; Research Institute for Medicine and Chemistry Inc.  
 SO PCT Int. Appl., 28 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-56  
 ICS A61K031-575; C07J041-00; A61P035-00  
 CC 32-5 (Steroids)  
 Section cross-reference(s): 1, 2, 63

FAN.CNT 1

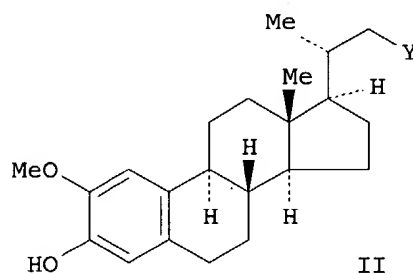
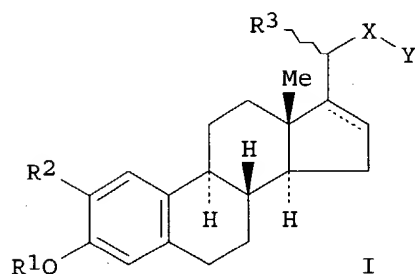
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092100	A1	20021121	WO 2002-GB2210	20020513
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI US 2001-290013P	P	20010511		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002092100	ICM	A61K031-56
	ICS	A61K031-575; C07J041-00; A61P035-00

OS MARPAT 137:370278

GI



AB Pregna-1,3,5(10)-triene derivs., such as I [R1 = H, hydroxy protecting group; R2 = OH, CHO, alkoxy, alkenyl, alkyl, etc.; R3 =  $\alpha$ -,  $\beta$ -Me; X = C1-3 alkylene group, bond; Y = C(R4)(R5)NR6R7; R4, R5 = H, alkyl, alkenyl and alkynyl groups, such that the total carbon content of R4 and R5 does not exceed three atoms; R6 = H, aliphatic or araliph. organic group, acyl, etc.; C16-C17 = saturated, unsatd.], were prepared for a variety of therapeutic uses, such as modulating cell activity, including

antiproliferative and antiangiogenic effects. Thus, pregna-1,3,5(10)-triene derivs. II (Y = NH<sub>2</sub>, NHCOME) were prepared via a multistep synthetic series starting from 2-methoxy-3-[[tris(1-methylethyl)silyl]oxy]-estra-1,3,5(10)-trien-17-one and ethyltriphenylphosphonium bromide.

Pharmaceutical compns. of the prepared compds. were discussed, but specific pharmaceutical activity testing data was not presented.

ST norpregnatriene prepn antiproliferative antiangiogenic agent

IT Mental disorder

(cognitive, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Blood coagulation

Cognition

(disorder, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Transplant and Transplantation

(graft-vs.-host reaction, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Anti-inflammatory agents

Anticholesteremic agents

Antitumor agents

Cognition enhancers

Contraceptives

Immunomodulators

(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Arthritis

(psoriatic arthritis, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Mental disorder

(senile psychosis, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Asthma

Autoimmune disease

Bone, disease

Hypercholesterolemia

Hyperplasia

Hypertension

Inflammation

Neoplasm

Rheumatoid arthritis

Skin, disease

Transplant rejection

(treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT 4736-60-1, Ethyltriphenylphosphonium iodide 305812-67-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT 229486-17-3P 305812-87-7P 305812-99-1P 372952-47-1P

372952-49-3P 372952-50-6P 475486-81-8P 475486-82-9P 475486-83-0P

475486-84-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT 475486-79-4P 475486-80-7P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

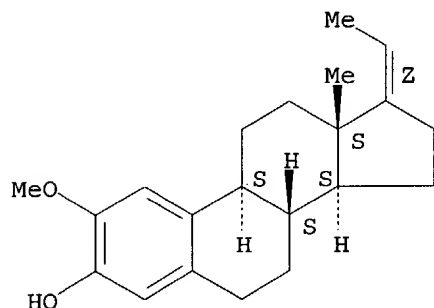
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Christopher, M; WO 0068246 A 2000 HCAPLUS

(2) Christopher, M; WO 0185755 A 2001 HCAPLUS  
 (3) Cushman, M; JOURNAL OF MEDICINAL CHEMISTRY 1995, V38(12), P2041 HCAPLUS  
 (4) Jacques, P; US 3291690 A 1966  
 IT 229486-17-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of  
 therapeutic uses)  
 RN 229486-17-3 HCAPLUS  
 CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L31 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2001:833342 HCAPLUS  
 DN 135:358085  
 ED Entered STN: 16 Nov 2001  
 TI Preparation of 2-substituted pregna-1,3,5(10)-triene and  
 chola-1,3,5(10)-triene derivatives with antiproliferative and  
 antiangiogenic activity  
 IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Pechet,  
 Maurice Murdoch; Gile, Michael  
 PA Marsden, John Christopher, UK; Research Institute for Medicine and  
 Chemistry Inc.  
 SO PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J041-00  
 ICS A61K031-57; C07J009-00; C07J013-00; C07J051-00; A61K031-575;  
 A61P005-30; A61P035-00  
 CC 32-5 (Steroids)  
 Section cross-reference(s): 1, 63

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085755	A1	20011115	WO 2001-GB2103	20010511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				



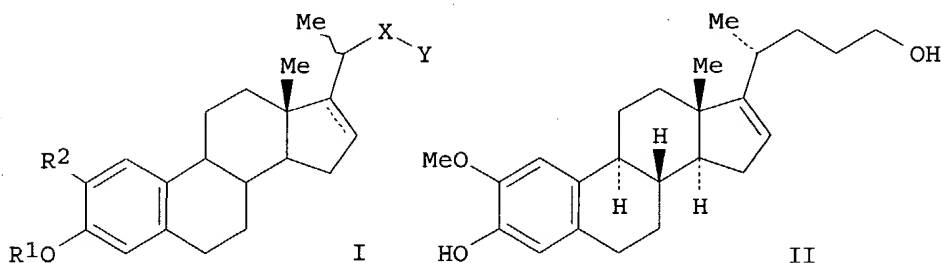
EP 1287017	A1	20030305	EP 2001-928120	20010511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003532737	T2	20031105	JP 2001-582354	20010511
NZ 523042	A	20040528	NZ 2001-523042	20010511
ZA 2002009060	A	20040209	ZA 2002-9060	20021107
NO 2002005392	A	20030109	NO 2002-5392	20021111
US 2003158167	A1	20030821	US 2003-275257	20030313
PRAI US 2000-203462P	P	20000511		
WO 2001-GB2103	W	20010511		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001085755	ICM	C07J041-00
	ICS	A61K031-57; C07J009-00; C07J013-00; C07J051-00; A61K031-575; A61P005-30; A61P035-00

OS MARPAT 135:358085

GI



AB Compds. of formula I [R1 = H, protecting group; R2 = OH, alkoxy, CHO, alkenyl, etc.; X = alkylene, bond; Y = CHO, (substituted) CH2OH, etc.] are prepared which exhibit potent cell modulating activity, including antiproliferative and antiangiogenic effects. Thus, 2-methoxy-3-triisopropylsilyloxy-19-norpregn-1,3,5(10),17(20)Z-tetraene (preparation given) is reacted with Me acrylate, reduced with LiAlH<sub>4</sub>, and desilylated with TBAF to give II.

ST pregnatriene deriv prepn antiproliferative antiangiogenic; cholatriene deriv prepn antiproliferative antiangiogenic; antiproliferative pregnatriene cholatriene deriv; antiangiogenic pregnatriene cholatriene deriv

IT Angiogenesis inhibitors  
Antitumor agents

(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT Proliferation inhibition

(proliferation inhibitors; preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 372952-25-5P 372952-27-7P 372952-29-9P 372952-30-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 372952-23-3P 372952-24-4P 372952-28-8P 372952-31-3P 372952-32-4P  
372952-33-5P 372952-34-6P 372952-35-7P 372952-36-8P 372952-37-9P  
372952-38-0P 372952-39-1P 372952-40-4P 372952-41-5P 372952-42-6P  
372952-43-7P 372952-44-8P 372952-45-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 96-33-3, Methyl acrylate 305812-67-3 372952-58-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 229486-17-3P 305812-87-7P 305812-89-9P 305812-91-3P

305812-97-9P 372952-46-0P 372952-47-1P 372952-48-2P 372952-49-3P

372952-50-6P 372952-51-7P 372952-52-8P 372952-53-9P 372952-54-0P

372952-55-1P 372952-56-2P 372952-57-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Cushman, M; JOURNAL OF MEDICINAL CHEMISTRY 1995, V38(12), P2041 HCAPLUS

(2) Marsden, J; WO 0068246 A 2000 HCAPLUS

(3) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A HCAPLUS

(4) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A HCAPLUS

(5) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A HCAPLUS

(6) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A HCAPLUS

(7) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A HCAPLUS

(8) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A 1979 HCAPLUS

(9) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A 1979 HCAPLUS

(10) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A 1979 HCAPLUS

(11) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A 1979 HCAPLUS

(12) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A 1979 HCAPLUS

(13) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063

(14) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063

(15) Ruggieri, P; US 3562260 A 1971 HCAPLUS

IT 229486-17-3P

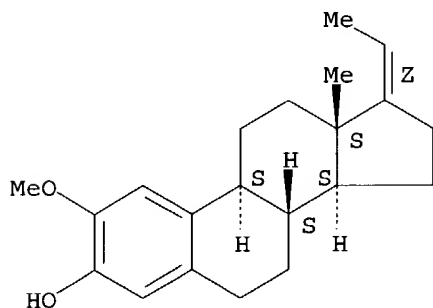
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RN 229486-17-3 HCAPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L31 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:283974 HCAPLUS

DN 134:295993

ED Entered STN: 20 Apr 2001  
 TI Estradiol conjugates and their therapeutic applications  
 IN Stewart, Alastair George; McAllister, David James; Collis, Maree Patricia;  
 Robertson, Alan Duncan  
 PA University of Melbourne, Australia  
 SO PCT Int. Appl., 57 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J001-00  
 ICS A61K047-36; A61K047-42; A61K047-48; A61P009-00; A61P035-00  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 1, 2, 33  
 FAN.CNT 1

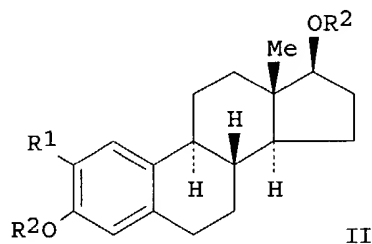
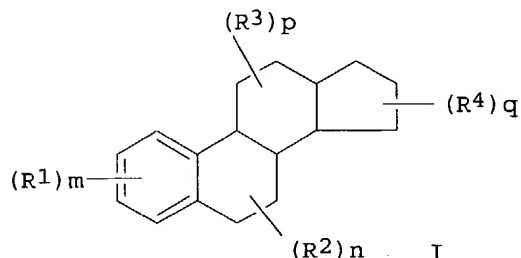
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001027132	A1	20010419	WO 2000-AU1244	20001013
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1226154	A1	20020731	EP 2000-969105	20001013
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003511461	T2	20030325	JP 2001-530350	20001013
	ZA 2002002622	A	20030304	ZA 2002-2622	20020404
PRAI	AU 1999-3425	A	19991014		
	WO 2000-AU1244	W	20001013		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001027132	ICM	C07J001-00
	ICS	A61K047-36; A61K047-42; A61K047-48; A61P009-00; A61P035-00

OS MARPAT 134:295993

GI



AB The invention discloses the preparation of conjugated prodrug of estradiol compound I (R1-R4 = H, OH, halo, alkyl, alkenyl, alkynyl, cycloalkyl, amino, aryl, keto, hydrazono, oximino, carbohydrate, peptide, etc.; m,n,p,q = 0-3), a pharmaceutically acceptable salt or in vivo hydrolyzable ester, amide carbonate or carbamate thereof, in the treatment of conditions associated with enhanced angiogenesis or accelerated cell division, such as cancer, and inflammatory conditions such as asthma and rheumatoid

arthritis and hyperproliferative skin disorders including psoriasis. Thus, II [R1 = OMe, R2 = H (III)] was prepared via multi-step reaction sequence starting from  $\beta$ -estradiol II (R1-R2 = H). In human airway fibroblasts thrombin-stimulated increases in cell number were reduced to  $12 \pm 8\%$  of the control response by III.

ST estradiol conjugate prodrug prepn angiogenesis inhibitor

IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(conjugates; preparation of peptide conjugated prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Partition

(for the measurement of relative solubilities of estradiol conjugates)

IT Glycosides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(glucuronides, estrogenic; preparation of glucuronide prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Estrogens

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(hydroxy, glucuronides; preparation of glucuronide prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Fluorometry

(in determination of relative solubilities of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Antitumor agents

(preparation of conjugated prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Antiasthmatics

Rheumatoid arthritis

(preparation of conjugated prodrug of estradiol compds. for the treatment of inflammatory conditions such as asthma and rheumatoid arthritis)

IT Psoriasis

(preparation of conjugated prodrug of estradiol compds. for the treatment psoriasis)

IT Estrogen receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(preparation of estradiol conjugates and their binding with rat uterine cytosol estrogen receptor)

IT DNA formation

(preparation of estradiol conjugates for regulation of DNA synthesis)

IT Respiratory tract

(preparation of estradiol conjugates for regulation of airway mesenchymal cell number)

IT Angiogenesis inhibitors

Anti-inflammatory agents

(preparation of estradiol conjugates for the treatment of conditions associated

with enhanced angiogenesis or accelerated cell division)

IT Estrogens

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of estradiol conjugates for the treatment of conditions associated

with enhanced angiogenesis or accelerated cell division)

IT Galactosides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of galactoside prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Drug delivery systems

(prodrugs; preparation of conjugated prodrug of an estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Proliferation inhibition

(proliferation inhibitors; preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Skin, disease

(proliferative; preparation of conjugated prodrug of estradiol compds. for the treatment of hyperproliferative skin disorders)

IT 7291-57-8P 69540-62-1P 334791-42-3P 334791-45-6P 334791-46-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of estradiol conjugates for the treatment of conditions

associated

with enhanced angiogenesis or accelerated cell division)

IT 171064-21-4P 334791-43-4P 334791-47-8P 334791-49-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of estradiol conjugates for the treatment of conditions

associated

with enhanced angiogenesis or accelerated cell division)

IT 9001-45-0,  $\beta$ -Glucuronidase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(preparation of estradiol conjugates for the treatment of conditions

associated

with enhanced angiogenesis or accelerated cell division)

IT 52717-98-3P

RL: BYP (Byproduct); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of estradiol conjugates for the treatment of conditions

associated

with enhanced angiogenesis or accelerated cell division)

IT 513-78-0, Cadmium carbonate

RL: CAT (Catalyst use); USES (Uses)

(preparation of estradiol conjugates for the treatment of conditions

associated

with enhanced angiogenesis or accelerated cell division)

IT 50-28-2,  $\beta$ -Estradiol, reactions 100-39-0, Benzyl bromide

108-24-7, Acetic anhydride 3068-32-4 7803-57-8, Hydrazine hydrate 21085-72-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of estradiol conjugates for the treatment of conditions

associated

with enhanced angiogenesis or accelerated cell division)

IT 362-07-2P 69455-04-5P 69540-63-2P 83274-89-9P 159143-75-6P  
159143-76-7P 192062-05-8P 334791-44-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation of estradiol conjugates for the treatment of conditions  
associated

with enhanced angiogenesis or accelerated cell division)

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Berg, D; Hoppe-Seyler's Z Physiol Chem 1982, V363(7), P737 HCAPLUS
- (2) Holler, M; Acta Endocrinologica 1982, V100, P57 MEDLINE
- (3) Nakagawa, A; Chem Pharm Bull 1978, V26(11), P3567 HCAPLUS
- (4) Nambara, T; Chem Pharm Bull 1976, V24(3), P421 HCAPLUS
- (5) Nambara, T; Chem Pharm Bull 1977, V25(5), P942 HCAPLUS
- (6) Ohkubo, T; Steroids 1990, V55(3), P128 HCAPLUS
- (7) Rohle, G; Hoppe-Seyler's Z Physiol Chem 1974, V355, P490 MEDLINE
- (8) Spiegelhalder, B; Journal of Steroid Biochemistry 1976, V7, P749 HCAPLUS
- (9) Stalford, A; Steroids 1997, V62, P750 HCAPLUS
- (10) Takanashi, K; Bunseki Kagaku 1995, V44(10), P793 HCAPLUS
- (11) The Children's Medical Center Corporation; WO 9504535 1995 HCAPLUS
- (12) Watanabe, K; Chem Pharm Bull 1982, V30(9), P3231 HCAPLUS

IT 52717-98-3P

RL: BYP (Byproduct); RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)

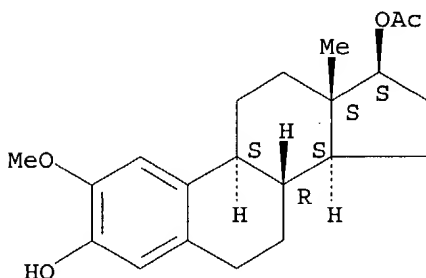
(preparation of estradiol conjugates for the treatment of conditions  
associated

with enhanced angiogenesis or accelerated cell division)

RN 52717-98-3 HCAPLUS

CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17 $\beta$ )-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:814500 HCAPLUS

DN 133:350395

ED Entered STN: 21 Nov 2000

TI Synthesis of cholestane compounds with a c17-alkyl side chain and an  
aromatic A-ring for use in cell modulating therapy

IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Ramgopal,  
Malathi; Kugabalusooriar, Sanga

PA Marsden, John; Christopher, UK; Research Institute for Medicine and  
Chemistry Inc.

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07J009-00

ICS C07J041-00; A61K031-575; C07J051-00; A61P017-02; A61P019-08;

A61P037-06; A61P029-00; A61P035-00; A61P021-00; A61P009-10;  
 A61P005-20; A61P017-00; A61P009-12; A61P019-02; A61P011-06;  
 A61P025-28; A61P015-18; A61P007-02; A61P003-06

CC 32-7 (Steroids)

Section cross-reference(s): 1, 2

FAN.CNT 1

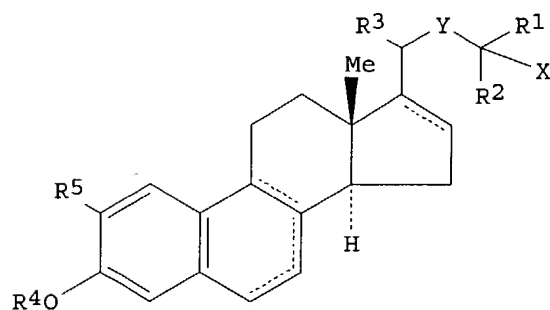
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000068246	A1	20001116	WO 2000-GB1813	20000511
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, GR, GU, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1179005	A1	20020213	EP 2000-927569	20000511
	EP 1179005	B1	20031119		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	AT 254629	E	20031215	AT 2000-927569	20000511
	PT 1179005	T	20040430	PT 2000-927569	20000511
	NZ 515482	A	20040528	NZ 2000-515482	20000511
	ES 2207509	T3	20040601	ES 2000-927569	20000511
	ZA 2001009272	A	20021128	ZA 2001-9272	20011109
	NO 2001005520	A	20020109	NO 2001-5520	20011112
PRAI	GB 1999-10934	A	19990511		
	WO 2000-GB1813	W	20000511		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000068246	ICM	C07J009-00
	ICS	C07J041-00; A61K031-575; C07J051-00; A61P017-02; A61P019-08; A61P037-06; A61P029-00; A61P035-00; A61P021-00; A61P009-10; A61P005-20; A61P017-00; A61P009-12; A61P019-02; A61P011-06; A61P025-28; A61P015-18; A61P007-02; A61P003-06

OS MARPAT 133:350395

GI



AB Synthesis of cholestane compds. (I) [R1 and R2, which may be the same or different, = alkyl, alkenyl, alkynyl; R3 = Me having  $\alpha$ - or  $\beta$ -configuration; R4 = H or an etherifying or esterifying group; R5 = H, OH, alkoxy; X = OR4, wherein R4 is as defined above, or NR6R7 wherein R6 = H, aliphatic or araliph. organic group, acyl group comprising aliphatic,

araliph. or aryl organic group linked to the nitrogen atom by way of a carbonyl group; R7 = H, alkyl; Y = (un)substituted alkylene, alkenylene, alkynylene; dotted lines signify that double bonds may be present at the 16(17)-position and/or either at the 6(7)- and 8(9)-positions or at the 7(8)-position] is disclosed for modulation of cell growth and differentiation, while having low calcemic activity. Thus, I [R1,R2 = Me; R3 =  $\alpha$ -Me; R4,R5 = H; X = NHAc; Y = (CH<sub>2</sub>)<sub>4</sub>;  $\Delta$ 16 double bond] is prepared by reaction of 3-triisopropylsilyloxy-19-norchol-1,3,5(10),16-tetraene-24-bromide with acetonitrile followed by reduction of nitrile to amine, methylation of amine with Me lithium, acetylation of the amino with acetic anhydride and desilylation with TBAF.

- ST cholestane analog prepn cell growth modulation differentiation; low calcemic activity cholestane analog
- IT Steroids, preparation  
Steroids, preparation  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(aromatic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)
- IT Transplant and Transplantation  
(host-vs.-graft reaction; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)
- IT Arthritis  
(psoriatic arthritis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)
- IT Hyperparathyroidism  
(secondary; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)
- IT Mental disorder  
(senile psychosis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)
- IT Heart, disease  
(spondylitic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)
- IT Aromatic hydrocarbons, preparation  
Aromatic hydrocarbons, preparation  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(steroids; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)
- IT Anti-inflammatory agents  
Antitumor agents  
Asthma  
Autoimmune disease  
Blood coagulation  
Bone, disease  
Burn  
Fertility  
Hyperplasia  
Hypertension  
Intestine, disease  
Muscle, disease  
Rheumatoid arthritis  
Skin, disease  
Transplant rejection  
Wound healing  
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)
- IT 57-88-5, Cholest-5-en-3-ol (3 $\beta$ )-, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)



(blood reduction; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 9002-64-6, Parathyroid hormone  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (suppression; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 305812-17-3P 305812-18-4P 305812-52-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 305812-19-5P 305812-20-8P 305812-21-9P 305812-22-0P 305812-23-1P  
 305812-24-2P 305812-25-3P 305812-26-4P 305812-27-5P 305812-28-6P  
 305812-29-7P 305812-30-0P 305812-31-1P 305812-32-2P 305812-33-3P  
 305812-34-4P 305812-35-5P 305812-36-6P 305812-37-7P 305812-38-8P  
 305812-39-9P 305812-40-2P 305812-41-3P 305812-42-4P 305812-43-5P  
 305812-44-6P 305812-45-7P 305812-46-8P 305812-47-9P 305812-48-0P  
 305812-49-1P 305812-50-4P 305812-51-5P 305812-53-7P 305812-54-8P  
 305812-55-9P 305812-56-0P 305812-57-1P 305812-58-2P 305812-59-3P  
 305812-60-6P 305812-61-7P 305812-62-8P 305812-63-9P 305812-64-0P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

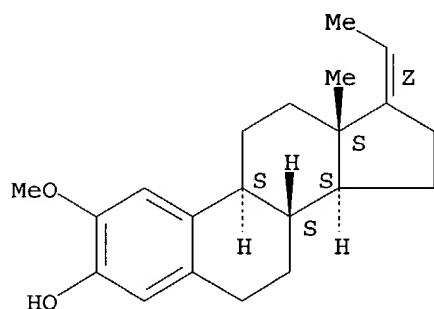
IT 74-88-4, Methyl iodide, reactions 75-03-6, Ethyl iodide 75-05-8, Acetonitrile, reactions 78-77-3, Isobutyl bromide 96-33-3 98-88-4, Benzoyl chloride 103-80-0, Phenylacetyl chloride 106-96-7, Propargyl bromide 474-87-3 517-09-9 867-13-0 922-67-8, Methyl propiolate 1439-36-7, 1-Triphenylphosphoranylidene-2-propanone 3234-64-8, 1,1-Diethylpropargylamine 4736-60-1, Ethyl triphenylphosphonium iodide 7103-48-2, Estrone-3-tetrahydropyranyl ether 17963-41-6 305812-65-1 305812-66-2 305812-67-3 305812-69-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 229486-17-3P 305812-70-8P 305812-71-9P 305812-72-0P  
 305812-73-1P 305812-75-3P 305812-76-4P 305812-77-5P 305812-79-7P  
 305812-81-1P 305812-83-3P 305812-85-5P 305812-87-7P 305812-89-9P  
 305812-91-3P 305812-93-5P 305812-95-7P 305812-97-9P 305812-99-1P  
 305813-01-8P 305813-03-0P 305813-05-2P 305813-07-4P 305813-09-6P  
 305813-10-9P 305813-12-1P 305813-14-3P 305813-15-4P 305813-16-5P  
 305813-17-6P 305813-19-8P 305813-20-1P 305813-21-2P 305813-22-3P  
 305813-23-4P 305813-25-6P 305813-26-7P 305813-27-8P 305813-28-9P  
 305813-30-3P 305813-32-5P 305813-34-7P 305813-36-9P 305813-38-1P  
 305813-39-2P 305813-40-5P 305813-41-6P 305813-42-7P 305813-43-8P  
 305813-44-9P 305813-45-0P 305813-46-1P 305813-47-2P 305813-48-3P  
 305813-49-4P 305813-50-7P 305813-51-8P 305813-52-9P 305813-53-0P  
 305813-54-1P 305813-55-2P 305813-56-3P 305813-57-4P 305813-58-5P  
 305813-59-6P 305813-60-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
 (1) Escalera; 1993, 7, HCAPLUS  
 (2) Escalera; J STEROID BIOCHEM MOL BIOL 1993, V45(4), P257 HCAPLUS  
 (3) Laing, S; US 3717627 A 1973  
 (4) Lajeunesse; 1994, 23, HCAPLUS  
 (5) Lajeunesse; BONE MINER 1994, V24(1), P1 HCAPLUS

(6) Liel; 1992, 25, HCAPLUS  
 (7) Liel; ENDOCRINOLOGY (BALTIMORE) 1992, V130(5), P2597 HCAPLUS  
 (8) Mountford; 1999, 8, HCAPLUS  
 (9) Mountford; EXP HEMATOL (N Y) 1999, V27(3), P451 HCAPLUS  
 (10) Ruggieri, P; US 3562260 A 1971 HCAPLUS  
 IT 229486-17-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (synthesis of cholestane compds. with a c17-alkyl side chain and an  
 aromatic A-ring for use in cell modulating therapy)  
 RN 229486-17-3 HCAPLUS  
 CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L31 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:460438 HCAPLUS  
 DN 131:88083  
 ED Entered STN: 28 Jul 1999  
 TI Preparation of estrone sulfamate inhibitors of estrone sulfatase  
 IN Tanabe, Masato; Peters, Richard H.; Chao, Wan-Ru; Shigeno, Kazuhiko  
 PA SRI International, USA  
 SO PCT Int. Appl., 102 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English  
 IC ICM C07J041-00  
 ICS A61K031-565; A61K031-57; A61K031-575  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 2, 63

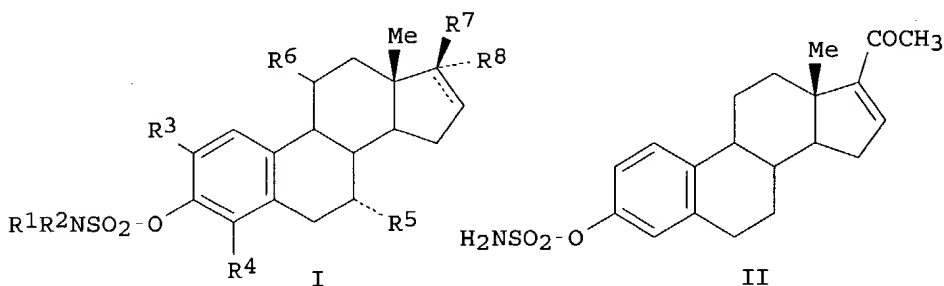
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9933858	A2	19990708	WO 1998-US27333	19981221
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6046186	A	20000404	US 1997-997416	19971224
	CA 2318349	AA	19990708	CA 1998-2318349	19981221
	AU 9919416	A1	19990719	AU 1999-19416	19981221
	AU 751732	B2	20020829		
	EP 1042354	A2	20001011	EP 1998-964243	19981221
	EP 1042354	B1	20040303		
	R: DE, FR, GB, IT, NL				
	JP 2001527089	T2	20011225	JP 2000-526534	19981221
	EP 1405860	A1	20040407	EP 2003-28361	19981221
	R: DE, FR, GB, IT, NL				

PRAI US 1997-997416 A 19971224  
 EP 1998-964243 A3 19981221  
 WO 1998-US27333 W 19981221

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9933858	ICM	C07J041-00
	ICS	A61K031-565; A61K031-57; A61K031-575
WO 9933858	ECLA	C07J041/00B; C07J041/00C40; C07J041/00C70
US 6046186	ECLA	C07J041/00B; C07J041/00C40; C07J041/00C70
EP 1405860	ECLA	C07J041/00B; C07J041/00C40; C07J041/00C70
OS MARPAT 131:88083		
GI		



AB Novel compds. of formula I [R<sup>1</sup>, R<sup>2</sup> = H, alkyl, etc.; R<sup>3</sup> = H, CN, NO<sub>2</sub>, COOH, alkoxy, carbonyl, etc.; R<sup>4</sup> = H, NO<sub>2</sub>, (substituted) amino; R<sup>5</sup>, R<sup>6</sup> = H, alkyl; R<sup>7</sup>, R<sup>8</sup> = H, alkyl, alkenyl, alkynyl, alkoxy, acyl, acyloxy, etc.; R<sup>7</sup>, R<sup>8</sup> = oxo, alkylidene, etc.] are prepared as inhibitors of estrone sulfatase. Thus, II is prepared from ethynylestradiol in 4 steps. and showed estrone sulfatase inhibitory activity of IC<sub>50</sub> = 21 pM. Pharmaceutical compns. and methods for using I to treat estrogen-dependent disorders are provided.

ST estrone sulfamate prepn estrone sulfatase inhibitor

IT Estrogens  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (antiestrogens; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT Antitumor agents  
 (preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 59298-96-3, Estrone sulfatase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (inhibitors; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 185910-34-3P 185910-42-3P 208924-86-1P 208924-87-2P 229485-78-3P  
 229485-79-4P 229485-80-7P 229485-81-8P 229485-82-9P 229485-83-0P  
 229485-84-1P 229485-85-2P 229485-86-3P 229485-87-4P 229485-88-5P  
 229485-89-6P 229485-90-9P 229485-91-0P 229485-92-1P 229485-93-2P  
 229485-94-3P 229485-95-4P 229485-96-5P 229485-97-6P 229485-98-7P  
 229485-99-8P 229486-00-4P 229486-01-5P 229486-02-6P 229486-03-7P  
 229486-04-8P 229486-05-9P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 50-28-2, Estradiol, reactions 53-16-7, Estrone, reactions 57-63-6, Ethynylestradiol 108-01-0, N,N-Dimethylethanolamine 109-77-3, Malononitrile 362-08-3 867-13-0, Triethylphosphonoacetate 1779-51-7,

Butyltriphenylphosphonium bromide 4584-46-7 5407-04-5 6228-47-3,  
 Propyltriphenylphosphonium bromide 7678-95-7 67530-18-1 229486-27-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 858-98-0P 1667-98-7P 4736-62-3P 5774-17-4P 5779-47-5P 5976-73-8P  
 5976-74-9P 6599-97-9P 13879-55-5P 13879-57-7P 14030-45-6P  
 14846-63-0P 14982-15-1P 15001-40-8P 22787-09-3P 23880-59-3P  
 31559-52-1P 57711-40-7P 59077-04-2P, 19-Norpregna-1,3,5(10)-trien-3-ol  
 59452-15-2P 59452-16-3P, 19,21-Dinorchola-1,3,5(10)-trien-3-ol  
 64215-82-3P 67519-62-4P 71716-18-2P 96111-26-1P 101766-63-6P  
 115208-23-6P 115387-92-3P 116627-15-7P 116627-20-4P 120574-27-8P  
 120574-28-9P 165619-18-1P 165619-19-2P 165619-20-5P 185910-40-1P  
 206442-55-9P 208758-44-5P 208758-45-6P 208758-46-7P 208758-49-0P  
 208758-50-3P 229486-06-0P 229486-07-1P 229486-08-2P 229486-09-3P  
 229486-10-6P 229486-11-7P 229486-12-8P 229486-13-9P 229486-14-0P  
 229486-15-1P 229486-16-2P **229486-17-3P 229486-18-4P**  
 229486-19-5P 229486-20-8P 229486-21-9P 229486-22-0P 229486-23-1P  
 229486-24-2P 229486-25-3P 229486-26-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT **229486-17-3P 229486-18-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

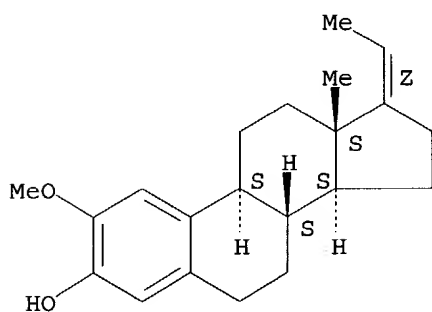
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

RN 229486-17-3 HCAPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.

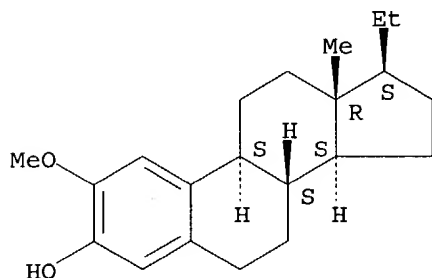
Double bond geometry as shown.



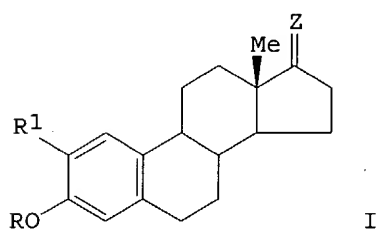
RN 229486-18-4 HCAPLUS

CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1978:121515 HCAPLUS  
 DN 88:121515  
 ED Entered STN: 12 May 1984  
 TI Synthesis of 2-methoxy-17 $\alpha$ -ethynylestradiol and its 3-methyl ether.  
 The Loudon ortho-hydroxylation reaction  
 AU Ei, Kei-Hwie; Teng, Ying-Hsiang; Wang, Wen-Jong; Chao, Hwa-Ming; Hsu,  
 Zhen-Pon  
 CS Szechwan Univ., Chengtu, Peop. Rep. China  
 SO Kexue Tongbao (Chinese Edition) (1977), 22(12), 539-42  
 CODEN: KHTPAT; ISSN: 0023-074X  
 DT Journal  
 LA Chinese  
 CC 32-3 (Steroids)  
 GI



AB Title estradiol (I, R = H, R1 = MeO, Z =  $\alpha$ -C.tplbond.CH,  $\beta$ -OH)  
 (II) was prepared by hydroxylation of I [R = 2,5-(PhCO)(O<sub>2</sub>N)C<sub>6</sub>H<sub>3</sub>, R1 = H, Z  
 =  $\alpha$ -H,  $\beta$ -OAc] (obtained by heating 17 $\beta$ -estradiol with  
 2,5-Cl(O<sub>2</sub>N)C<sub>6</sub>H<sub>3</sub>COPh followed by acetylation) with HOAc-concentrated H<sub>2</sub>SO<sub>4</sub> and  
 then H<sub>2</sub>O<sub>2</sub> and subsequent 2-O-methylation, hydrolysis, Jones oxidation,  
 reduction,  
 and ethynylation using of KC.tplbond.CH. 3-O-methylation of II with CH<sub>2</sub>N<sub>2</sub>  
 gave I (R = Me, R1 = MeO, Z =  $\alpha$ -C.tplbond.CH,  $\beta$ -OH).  
 ST ethynylmethoxyestradiol; Loudon hydroxylation estradiol; estradiol ethynyl  
 ethoxy methyl; steroid hydroxy unsatd  
 IT Steroids, preparation  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (17 $\beta$ -hydroxy-1,3,5-unsatd., preparation of, Loudon hydroxylation for)  
 IT Hydroxylation  
 (Loudon, of estradiol)  
 IT 26011-40-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (methylation of)  
 IT 65932-52-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and Jones oxidation of)  
 IT 65932-49-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and acetylation of)  
 IT 53-16-7P, preparation  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and ethynylation of)  
 IT 65932-51-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and hydrolysis of)  
 IT 22415-44-7P 38781-50-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and methylation of)

IT 65932-50-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and oxidation of)

IT 65932-53-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reduction of)

IT 362-07-2P 52717-98-3P 55236-35-6P 65975-87-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

IT 50-28-2, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with 2-chloro-5-nitrobenzophenone)

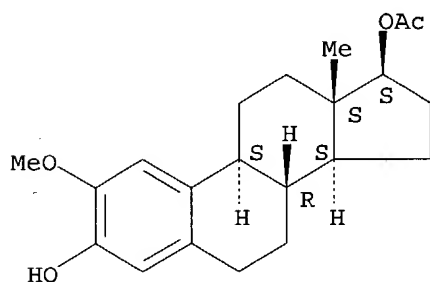
IT 34052-37-4  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with estradiol)

IT 52717-98-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 52717-98-3 HCAPLUS

CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17 $\beta$ )-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1974:404163 HCAPLUS

DN 81:4163

ED Entered STN: 12 May 1984

TI Synthesis of glucuronides of 2-hydroxylated estrogens and their methyl ethers

AU Roehle, Gerhard; Breuer, Heinz

CS Inst. Klin. Biochem., Bonn, Fed. Rep. Ger.

SO Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie (1974), 355(4), 490-4

CODEN: HSZPAZ; ISSN: 0018-4888

DT Journal

LA English

CC 33-3 (Carbohydrates)

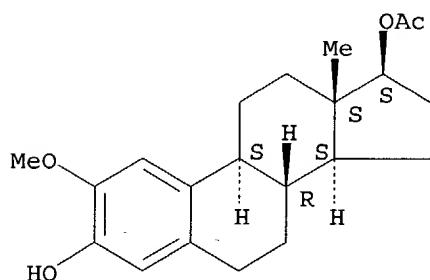
Section cross-reference(s): 32

AB The chemical synthesis of the phenolic  $\beta$ -D-glucuronides of 2-methoxy-17 $\beta$ -estradiol, 2-hydroxy-17 $\beta$ -estradiol (I) and its 3-Me ether was described. Thus, reaction of the 17-acetate of I with Me 2,3,4-tri-O-acetyl-1-bromo-1-deoxy- $\alpha$ -D-glucopyranuronate in the presence of Cd carbonate gave only the corresponding 2-glucuronide. Under the exptl. conditions employed, no 3-glucuronide was formed. The

selectivity of the glucuronidation reaction is not in accord. with the suggestion, made by J. Fishman et al. (1967), that the phenolic groups in ring A of 2-hydroxy estrogens may be chemical indistinguishable.

ST hydroxyestrogen glucuronidation; estrogen hydroxy glucuronidation  
 IT Steroids, preparation  
 RL: PREP (Preparation)  
     (hydroxyestradiol glucuronides)  
 IT 27736-75-0P 52718-00-0P 52718-01-1P 52718-02-2P 52719-25-2P  
 52745-31-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
     (preparation of)  
 IT 21085-72-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
     (reaction of, with hydroxyestrogens)  
 IT 23463-05-0 52717-98-3 52717-99-4  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
     (reaction of, with methyl bromodeoxyglucopyranuronates)  
 IT 52717-98-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
     (reaction of, with methyl bromodeoxyglucopyranuronates)  
 RN 52717-98-3 HCAPLUS  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17 $\beta$ )-  
     (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> => d all 126 tot hitstr

L26 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2003:719252 HCAPLUS  
 DN 139:224972  
 ED Entered STN: 14 Sep 2003  
 TI Synthesis of 2-methoxyestradiol derivatives and uses as antiangiogenic agents  
 IN Lavallee, Theresa M.; Pribluda, Victor S.; Simons, Jonathan; Mabjeesh, Nicola; Giannakakou, Paraskevi  
 PA Entremed, Inc., USA  
 SO PCT Int. Appl., 77 pp.  
     CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K  
 CC 2-4 (Mammalian Hormones)  
     Section cross-reference(s): 32

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003073985	A2	20030912	WO 2003-US5898	20030227
	WO 2003073985	A3	20031231		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-361267P P 20020301

CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

WO 2003073985 ICM A61K

- AB Compns. and methods for treating mammalian disease characterized by undesirable angiogenesis and for controlling a number of angiogenesis-related events, conditions, or substances, by administering derivs. of 2-methoxyestradiol of general formula (I) wherein the variables are defined in the specification.
- ST estrogen methoxyestradiol analogs angiogenesis inhibitor VEGF DR5 HIFalpha
- IT Apoptosis  
(2-ME2-induced; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT Cytokine receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(DR5 (death receptor 5); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT Transcription factors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(HIF-1α (hypoxia-inducible factor 1α); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT Blood vessel  
(endothelium; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT Transcriptional regulation  
(of HIF-1α, 2-ME2-inhibited; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT Angiogenesis  
Angiogenesis inhibitors  
Human  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT Estrogens  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT 127464-60-2, Vascular Endothelial Growth Factor  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT 362-07-2DP, 2-Methoxyestradiol, derivs. and analogs 362-07-2P, 2-Methoxyestradiol  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT 50-00-0, Formaldehyde, reactions 50-28-2D, Estradiol, derivs. and analogs 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 64-19-7, Acetic acid, reactions 67-68-5, Methyl sulfoxide, reactions

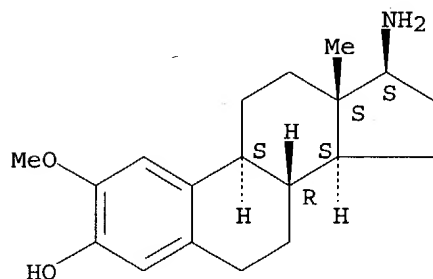




RN 431901-68-7 HCAPLUS

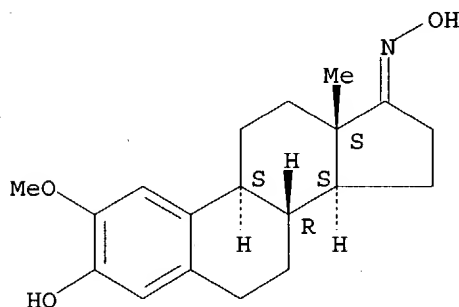
CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431901-69-8 HCAPLUS

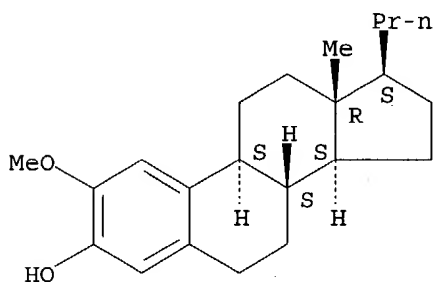
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

RN 431901-70-1 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

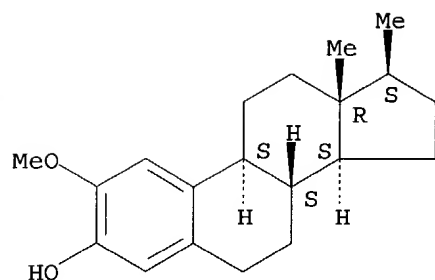
Absolute stereochemistry.



RN 431901-71-2 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

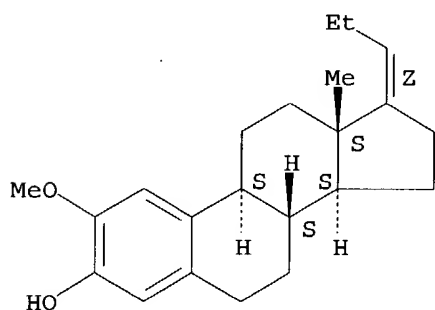
Absolute stereochemistry.



RN 431901-72-3 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

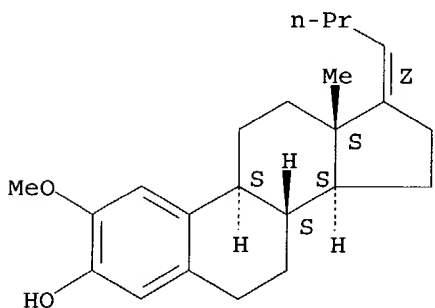
Absolute stereochemistry.  
Double bond geometry as shown.



RN 431901-77-8 HCAPLUS

CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

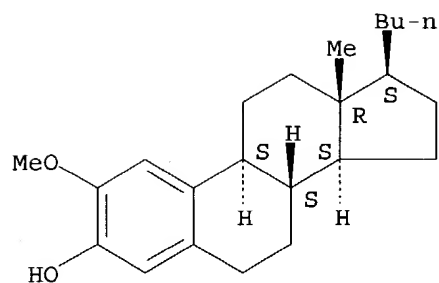
Absolute stereochemistry.  
Double bond geometry as shown.



RN 431901-78-9 HCAPLUS

CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

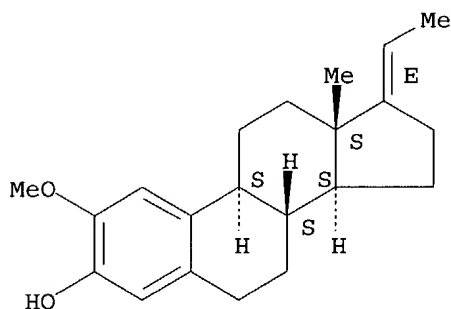
Absolute stereochemistry.



RN 594873-87-7 HCAPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L26 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:488275 HCAPLUS

DN 137:47357

ED Entered STN: 28 Jun 2002

TI Preparation of 2-methoxyestradiol derivatives as antiangiogenic agents

IN Agoston, Gregory E.; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor S.; Lavalley, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony M.

PA USA

SO U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 933,894.  
CODEN: USXXCO

DT Patent

LA English

IC ICM C07J041-00

ICS C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56;  
C07C247-00; A61K031-655; C07J009-00

NCL 552544000

CC 32-3 (Steroids)

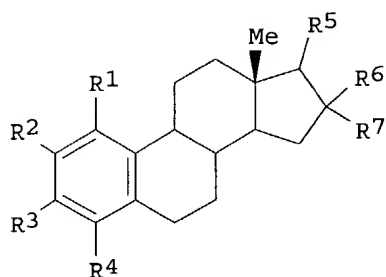
Section cross-reference(s): 1

FAN.CNT 2

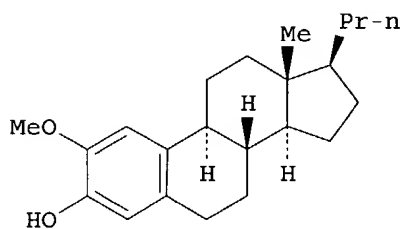
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002082433	A1	20020627	US 2001-939208	20010824 <--
PRAI	US 2000-641327	A2	20000818		
	US 2000-253385P	P	20001127		
	US 2000-255302P	P	20001213		
	US 2001-278250P	P	20010323		
	US 2001-933894	A2	20010821		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002082433	ICM	C07J041-00
	ICS	C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56; C07C247-00; A61K031-655; C07J009-00
	NCL	552544000
OS	MARPAT 137:47357	
GI		



I



II

- AB 2-Methoxyestradiol derivs. of formula I [R1, R4 = H, halo, CN, alkyl, OH, NH2, etc.; R2 = N3, CN, OMe, alkenyl, alkynyl, alkoxy, NH2, etc.; R3 = OH, OAc; R5 = alkyl, alkenyl, (di)alkylamino, OH, alkylene, etc.; R6, R7 = H, alkyl, alkenyl, alkynyl, halo, etc.] are prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol and propyltriphenylphosphonium bromide. The IC50 of II against MDA-MB-231 breast tumor cells was 51.31  $\mu$ M.
- ST methoxyestradiol deriv prepn antiangiogenic; estradiol deriv prepn antiangiogenic; antitumor methoxyestradiol deriv prepn; antimetabolic methoxyestradiol deriv prepn
- IT Structure-activity relationship  
(antitumor; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT Mitosis  
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT Angiogenesis inhibitors  
Antitumor agents  
Human  
Mammary gland, neoplasm  
Neoplasm  
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT 362-07-2, 2-Methoxyestradiol  
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)  
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 6301-87-7P 431901-72-3P  
431901-73-4P 431901-75-6P 431901-77-8P  
431901-91-6P  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT 1818-12-8P 4953-96-2P 6298-51-7P 6599-97-9P 7291-57-8P  
10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P 165619-07-8P  
165881-61-8P 229486-18-4P 431901-68-7P  
431901-69-8P 431901-70-1P 431901-71-2P

431901-74-5P 431901-78-9P 431901-87-0P 431901-90-5P  
 431901-92-7P 431901-93-8P 431901-94-9P 431901-95-0P 431901-96-1P  
 431901-97-2P 431901-98-3P 431901-99-4P 431902-00-0P 431902-01-1P  
 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P  
 431902-07-7P 431902-08-8P 431902-09-9P 438044-29-2P  
 438044-30-5P 438044-35-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-16-7, Estrone, reactions 106-95-6, Allyl bromide, reactions 1779-51-7, Butyltriphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7 6228-47-3, Propyltriphenylphosphonium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-81-4P  
 431901-82-5P 431901-83-6P 431901-84-7P 431901-85-8P 431901-89-2P  
 438044-31-6P 438044-32-7P 438044-33-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

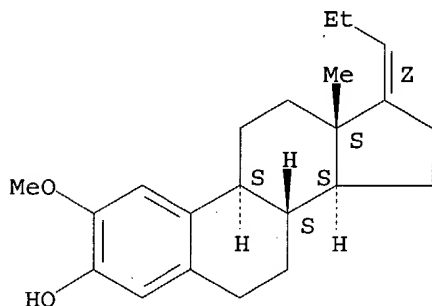
IT 431901-72-3P 431901-73-4P 431901-75-6P  
 431901-77-8P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 431901-72-3 HCAPLUS

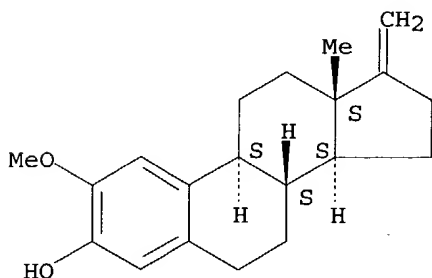
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)



RN 431901-73-4 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

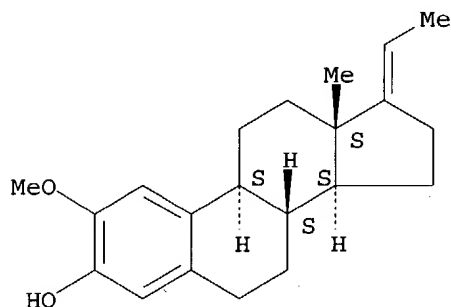
Absolute stereochemistry.



RN 431901-75-6 HCAPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

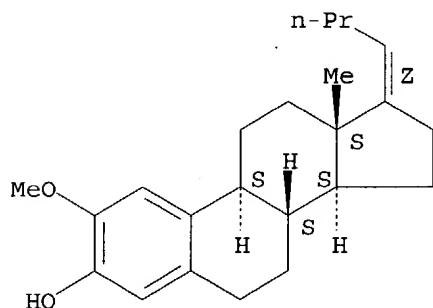
Absolute stereochemistry.  
Double bond geometry unknown.



RN 431901-77-8 HCAPLUS

CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



IT 229486-18-4P 431901-68-7P 431901-69-8P  
431901-70-1P 431901-71-2P 431901-74-5P  
431901-78-9P 438044-29-2P

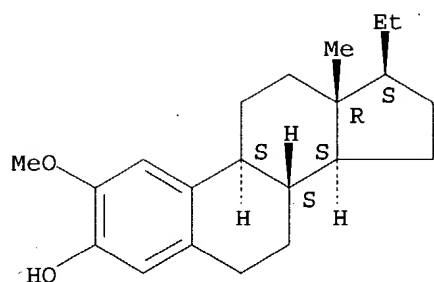
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 229486-18-4 HCAPLUS

CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

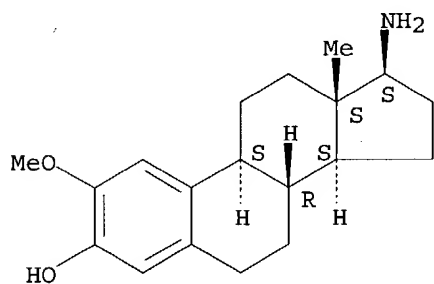
Absolute stereochemistry.



RN 431901-68-7 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

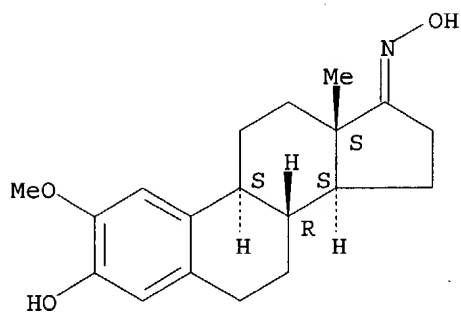


RN 431901-69-8 HCAPLUS

CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

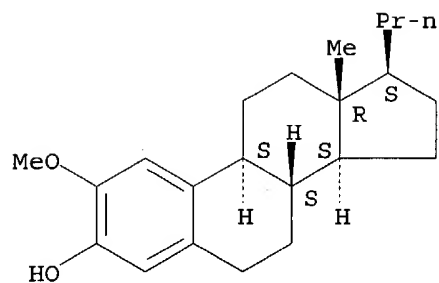


RN 431901-70-1 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

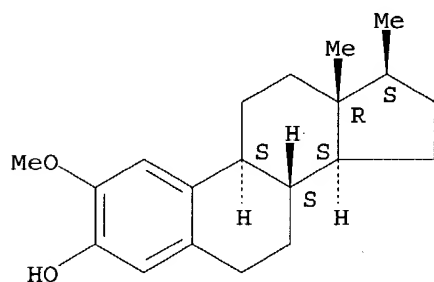




RN 431901-71-2 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

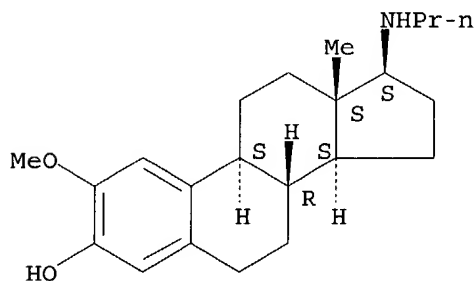
Absolute stereochemistry.



RN 431901-74-5 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

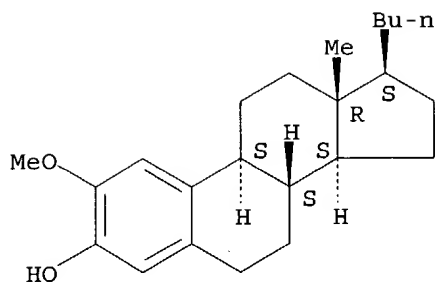
Absolute stereochemistry.



RN 431901-78-9 HCAPLUS

CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

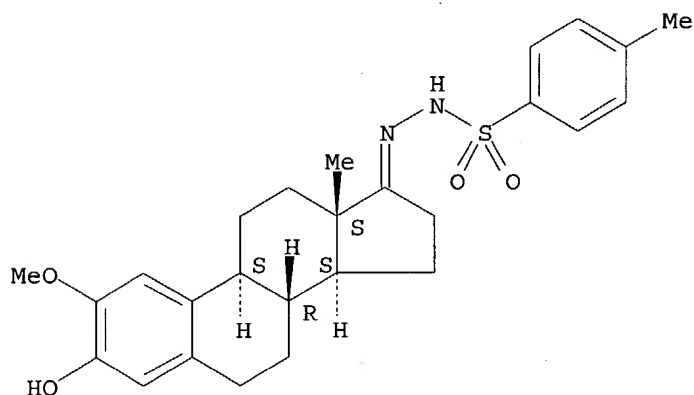
Absolute stereochemistry.



RN 438044-29-2 HCAPLUS

CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



L26 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:408687 HCAPLUS

DN 137:6309

ED Entered STN: 31 May 2002

TI Preparation of 2-methoxyestradiol analogs as antiangiogenic agents

IN Agoston, Gregory; Shah, Jamshed H.; Hunsucker,

Kimberly A.; Prihluda, Victor; Lavalley, Theresa M.

; Green, Shawn J.; Herbstritt, Christopher J.;

Zhan, Xiaoguo H.; Treston, Anthony

PA Entremed, Inc., USA

SO PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07J001-00

CC 32-3 (Steroids)

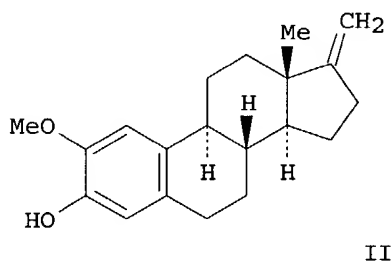
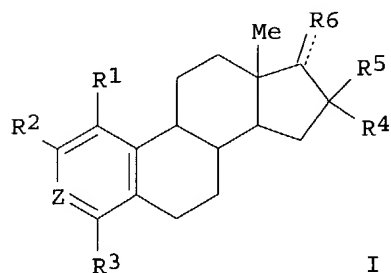
Section cross-reference(s): 1, 2, 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002042319	A2	20020530	WO 2001-US26490	20010824
	WO 2002042319	A3	20030313		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,				

CLASS

WO 2002042319 ICM C07J001-00  
OS MARPAT 137:6309  
GI



AB 2-Methoxyestradiol analogs, such as I [R1, R3 = H, halo, CN, alkyl, OH, CH2OH, NH2, alkylamino; R2 = N3, CN, C.tplbond.CR, C=CHR, C.tplbond.CH, OR, amino; R = H, alkyl; Z = COH, COAc; dashed bond = single bond or double bond; R6 = H, OH, O, oxime, amino, alkyl, alkenyl; R4, R5 = H, alkyl, alkenyl, alkynyl], were prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, 2-methoxyestradiol analog II was prepared by the reaction of methyltriphenylphosphonium bromide and 2-methoxyestrone. In vitro evaluation against MDA-MB-231 breast tumor cells and HUVEC endothelial cells, II showed IC50 0.24±0 and 0.19±0.19 resp.

ST methoxyestradiol deriv prepn antiangiogenic antitumor; estradiol methoxy deriv prepn antiangiogenic antitumor

IT Cell proliferation  
(inhibition; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mammary gland, neoplasm  
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

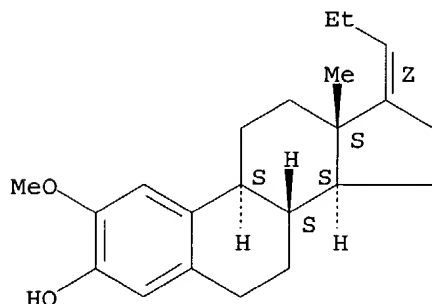
IT Antitumor agents  
(mammary gland; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors  
Human  
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Estrogens  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

- (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 431901-72-3P  
 431901-73-4P 431901-75-6P 431901-77-8P  
 431901-83-6P 431901-89-2P 431901-91-6P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
- (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT 1818-12-8P 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P  
 7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P  
 165619-07-8P 165881-61-8P 192062-02-5P 229486-18-4P  
 431901-68-7P 431901-69-8P 431901-70-1P  
 431901-71-2P 431901-74-5P 431901-76-7P  
 431901-78-9P 431901-82-5P 431901-84-7P 431901-86-9P  
 431901-87-0P 431901-88-1P 431901-92-7P 431901-93-8P 431901-94-9P  
 431901-95-0P 431901-96-1P 431901-97-2P 431901-98-3P 431901-99-4P  
 431902-00-0P 431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P  
 431902-05-5P 431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions 362-07-2, 2-Methoxyestradiol 1530-32-1, Ethyl triphenylphosphonium bromide 1779-49-3, Methyl triphenylphosphonium bromide 1779-51-7, Butyl triphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide 17640-15-2, Methyl cyanoformate  
 RL: RCT (Reactant); RACT (Reactant or reagent)
- (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-80-3P  
 431901-81-4P 431901-85-8P 431901-90-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
- (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- IT 431901-72-3P 431901-73-4P 431901-75-6P  
 431901-77-8P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
- (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
- RN 431901-72-3 HCAPLUS
- CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

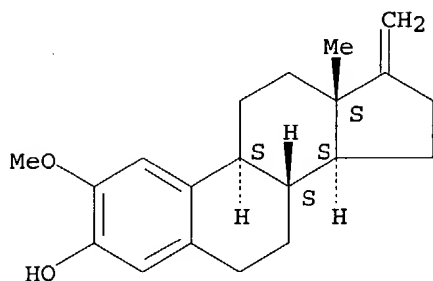
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 431901-73-4 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

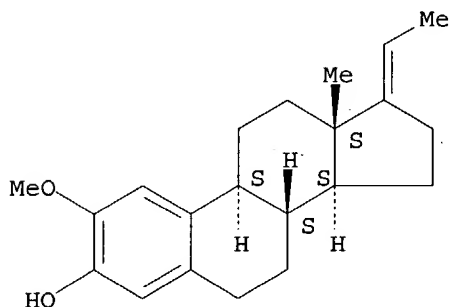


RN 431901-75-6 HCAPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

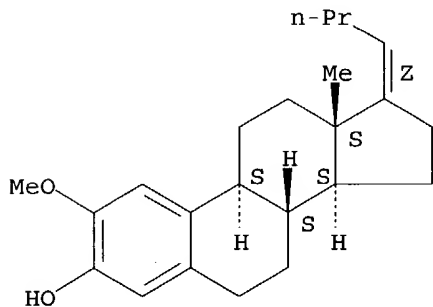


RN 431901-77-8 HCAPLUS

CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 229486-18-4P 431901-68-7P 431901-69-8P

431901-70-1P 431901-71-2P 431901-74-5P

431901-78-9P

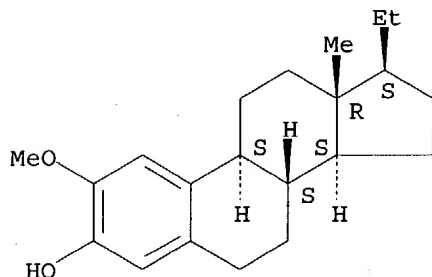
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 229486-18-4 HCAPLUS

CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

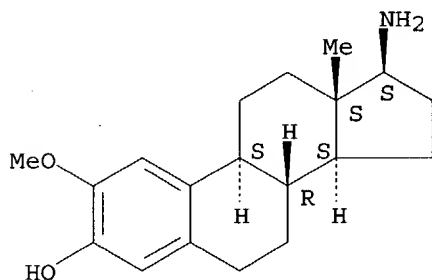
Absolute stereochemistry.



RN 431901-68-7 HCAPLUS

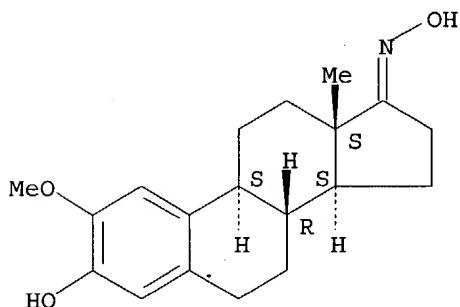
CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431901-69-8 HCAPLUS

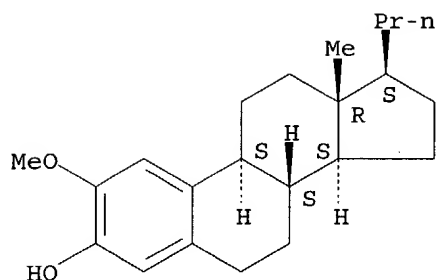
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

RN 431901-70-1 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

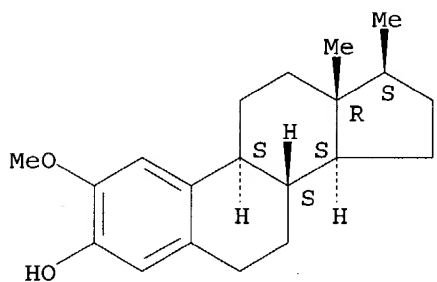
Absolute stereochemistry.



RN 431901-71-2 HCAPLUS

CN Estradiol, 17-methyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

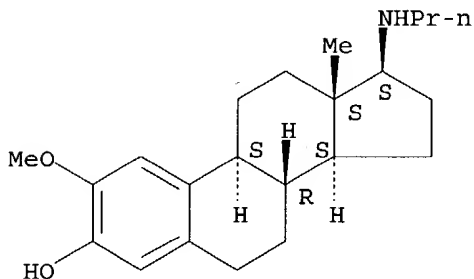
Absolute stereochemistry.



RN 431901-74-5 HCAPLUS

CN Estradiol, 17-(propylamino)-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

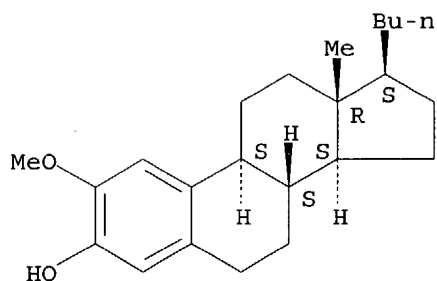
Absolute stereochemistry.



RN 431901-78-9 HCAPLUS

CN Estradiol, 17-(propylamino)-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE 'USPATFULL' ENTERED AT 14:07:42 ON 28 OCT 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 14:07:42 ON 28 OCT 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr tot 128

L28 ANSWER 1 OF 4 USPATFULL on STN

AN 2004:2032 USPATFULL

TI Systems and methods for rapid evaluation and design of molecules for predicted biological activity

IN Hendry, Lawrence B., Augusta, GA, UNITED STATES

PI US 2004002052 A1 20040101

AI US 2002-279546 A1 20021023 (10)

PRAI US 2001-344560P 20011023 (60)

US 2001-339954P 20011210 (60)

DT Utility

FS APPLICATION

LREP JOHN S. PRATT, ESQ, KILPATRICK STOCKTON, LLP, 1100 PEACHTREE STREET, SUITE 2800, ATLANTA, GA, 30309

CLMN Number of Claims: 38

ECL Exemplary Claim: 1

DRWN 16 Drawing Page(s)

LN.CNT 2883

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The computer-based systems and methods are for rapidly evaluating molecules for suspected biological activity and relative potency, and for designing molecules for desired biological activity. The systems and methods enable rapid screening of large molecular databases using one or more search engines designed to identify molecules predicted to possess specific biological activities.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 229486-17-3 431901-73-4

(as standard in construction of search engine for evaluation of substances for predicted antiangiogenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

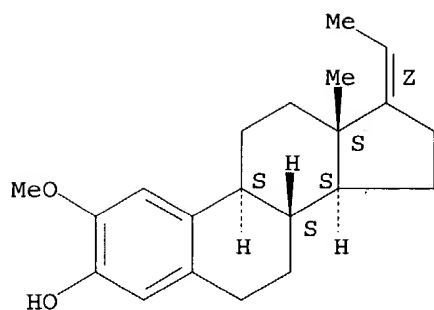
RN 229486-17-3 USPATFULL

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

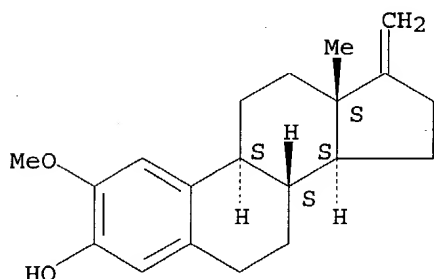




RN 431901-73-4 USPATFULL

CN Estr-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 2 OF 4 USPATFULL on STN

AN 2003:226354 USPATFULL

TI 2-substituted pregna-1,3,5(10) triene and chola-1,3,5(10) triene derivatives and their biological activity

IN Hesse, Robert Henry, Winchester, MA, UNITED STATES

Setty, Sundara Katugam Srinivasasetty, Cambridge, MA, UNITED STATES

Pechet, Maurice Murdoch, Cambridge, MA, UNITED STATES

Gile, Michael, Methuen, MA, UNITED STATES

PI US 2003158167 A1 20030821

AI US 2003-275257 A1 20030313 (10)

WO 2001-GB2103 20010511

DT Utility

FS APPLICATION

LREP BACON &amp; THOMAS, PLLC, 625 SLATERS LANE, FOURTH FLOOR, ALEXANDRIA, VA, 22314

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 978

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of formula (I) in which: R<sup>sup.1</sup> represents a hydrogen atom or an O-protecting group; R<sup>sup.2</sup> represents a hydroxyl, lower alkoxy, carboxaldehyde, lower alk-1-enyl or hydroxy- or lower alkoxy-substituted lower alkyl group; R<sup>sup.3</sup> represents a methyl group having  $\alpha$ - or  $\beta$ -configuration; X represents a C<sub>1-3</sub> alkylene group or a valence bond; Y represents a carboxaldehyde group or a group of formula --C(R<sup>sup.4</sup>)(R<sup>sup.5</sup>)OR<sup>sup.1</sup> where R<sup>sup.1</sup> is as defined above and R<sup>sup.4</sup> and R<sup>sup.5</sup>, which may be the same or different, are each selected from hydrogen atoms, alkyl, alkenyl and alkynyl groups such that the total carbon content of R<sup>sup.4</sup> and R<sup>sup.5</sup> does not exceed three atoms, with the proviso that X is a valence bond when both R<sup>sup.4</sup>

and R.sup.5 are other than hydrogen; and the dotted line signifies that a double bond may optionally be present at the 16(17)-position exhibit potent cell modulating activity, including antiproliferative and antiangiogenic effects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 229486-17-3P

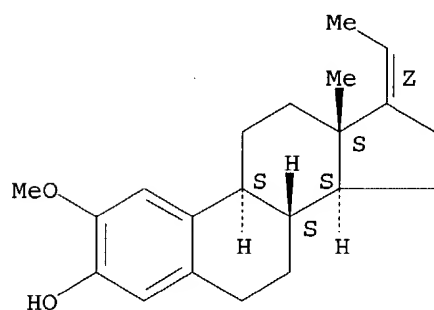
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RN 229486-17-3 USPATFULL

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L28 ANSWER 3 OF 4 USPATFULL on STN

AN 2002:157823 USPATFULL

TI Antiangiogenic agents

IN Agoston, Gregory E., Germantown, MD, UNITED STATES

Shah, Jamshed H., Brookeville, MD, UNITED STATES

Hunsucker, Kimberly A., Germantown, MD, UNITED STATES

Pribluda, Victor S., Silver Spring, MD, UNITED STATES

LaVallee, Theresa M., Rockville, MD, UNITED STATES

Green, Shawn J., Vienna, VA, UNITED STATES

Herbstritt, Christopher J., Rockville, VA, UNITED STATES

Zhan, Xiaoguo H., Montgomery Village, MD, UNITED STATES

Treston, Anthony M., Rockville, MD, UNITED STATES

PI US 2002082433 A1 20020627

AI US 2001-939208 A1 20010824 (9)

RLI Continuation-in-part of Ser. No. US 2001-933894, filed on 21 Aug 2001,  
PENDING Continuation-in-part of Ser. No. US 2000-641327, filed on 18 Aug  
2000, PENDING

PRAI US 2000-253385P 20001127 (60)

US 2000-255302P 20001213 (60)

US 2001-278250P 20010323 (60)

DT Utility

FS APPLICATION

LREP John S. Pratt, KILPATRICK STOCKTON LLP, Suite 2800, 1100 Peachtree  
Street, Atlanta, GA, 30309-4530

CLMN Number of Claims: 92

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2637

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compositions and methods for treating mammalian disease characterized by  
undesirable angiogenesis by administering derivatives of  
2-methoxyestradiol of the general formula: ##STR1##

wherein the variables are defined in the specification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

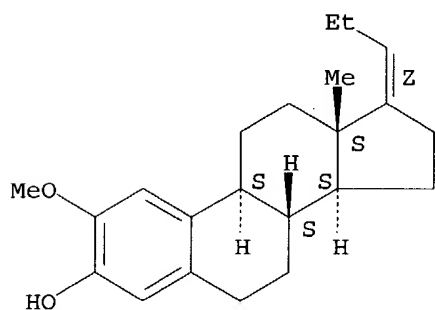
IT 431901-72-3P 431901-73-4P 431901-75-6P  
431901-77-8P

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 431901-72-3 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

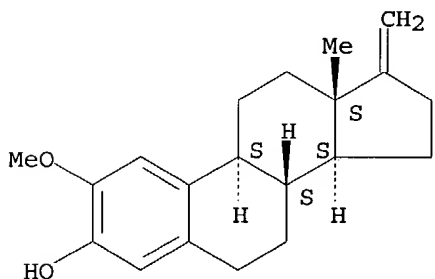
Absolute stereochemistry.  
Double bond geometry as shown.



RN 431901-73-4 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

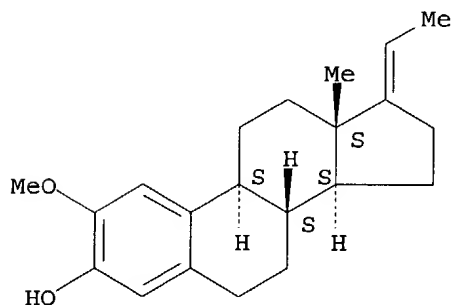
Absolute stereochemistry.



RN 431901-75-6 USPATFULL

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

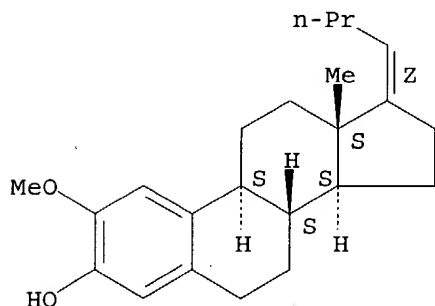
Absolute stereochemistry.  
Double bond geometry unknown.



RN 431901-77-8 USPATFULL

CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



IT 229486-18-4P 431901-68-7P 431901-69-8P

431901-70-1P 431901-71-2P 431901-74-5P

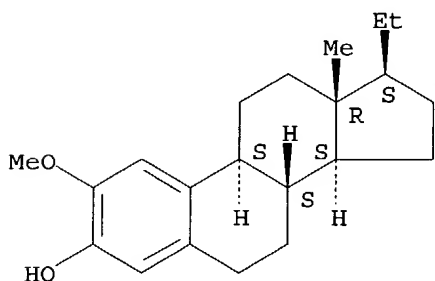
431901-78-9P 438044-29-2P

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 229486-18-4 USPATFULL

CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

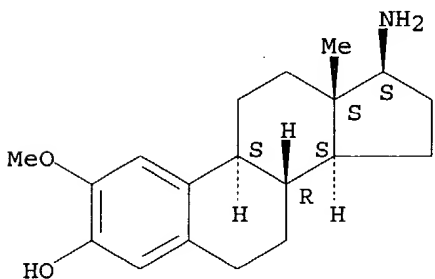
Absolute stereochemistry.



RN 431901-68-7 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17β)- (9CI) (CA  
INDEX NAME)

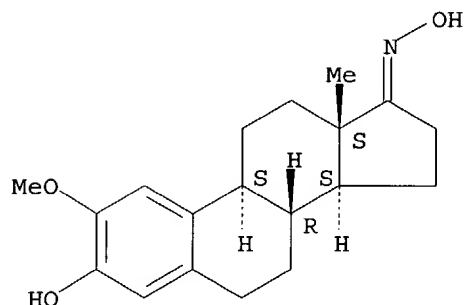
Absolute stereochemistry.



RN 431901-69-8 USPATFULL

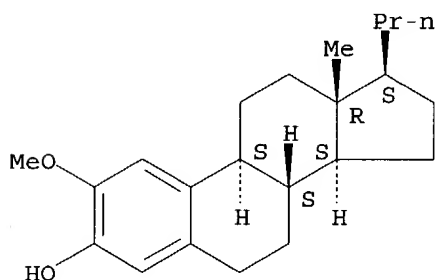
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



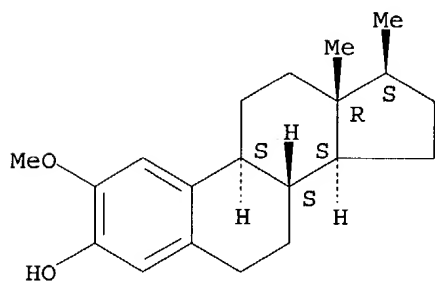
RN 431901-70-1 USPATFULL  
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



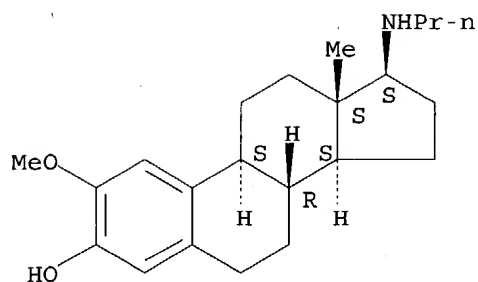
RN 431901-71-2 USPATFULL  
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431901-74-5 USPATFULL  
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17β)- (9CI) (CA INDEX NAME)

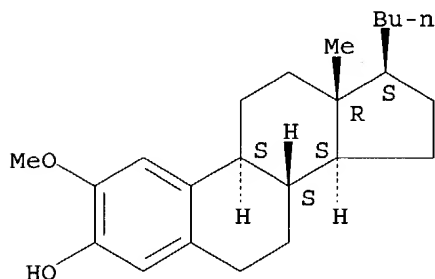
Absolute stereochemistry.



RN 431901-78-9 USPATFULL

CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

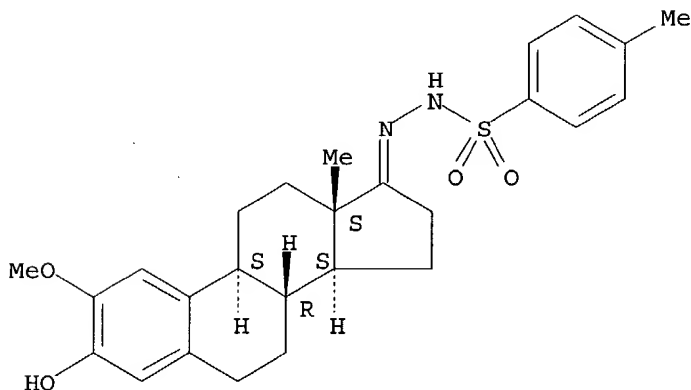


RN 438044-29-2 USPATFULL

CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



L28 ANSWER 4 OF 4 USPATFULL on STN

AN 2000:41031 USPATFULL

TI Estrone sulfamate inhibitors of estrone sulfatase, and associated pharmaceutical compositions and methods of use

IN Tanabe, Masato, Palo Alto, CA, United States  
Peters, Richard H., San Jose, CA, United States

Chao, Wan-Ru, Sunnyvale, CA, United States  
Shigeno, Kazuhiko, Saitama, CA, United States

PA SRI International, Menlo Park, CA, United States (U.S. corporation)

PI US 6046186 20000404  
 AI US 1997-997416 19971224 (8)  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Coleman, Brenda  
 LREP Reed, Dianne E. Reed & Associates  
 CLMN Number of Claims: 65  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 3007

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel compounds useful as inhibitors of estrone sulfatase are provided. The compounds have the structural formula (I) wherein  $r_1$  is an optional double bond,  $R_{sup.1}$  and  $R_{sup.2}$  are selected from the group consisting of hydrogen and lower alkyl, or together form a cyclic substituent (II) ##STR1## wherein Q is NH, O or  $CH_{sub.2}$ , and the other various substituents are as defined herein. Pharmaceutical compositions and methods for using the compounds of formula (I) to treat estrogen-dependent disorders are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

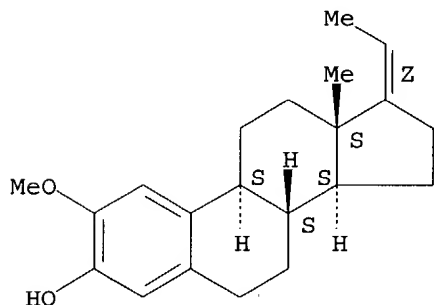
IT 229486-17-3P 229486-18-4P

(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

RN 229486-17-3 USPATFULL

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

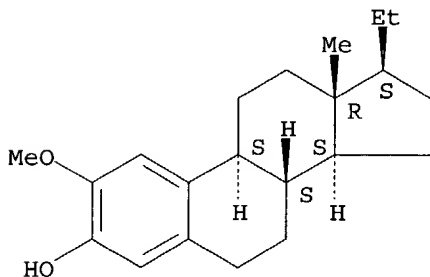
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 229486-18-4 USPATFULL

CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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(FILE 'HOME' ENTERED AT 13:43:08 ON 28 OCT 2004)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 13:43:14 ON 28 OCT 2004

FILE 'HCAPLUS' ENTERED AT 13:43:29 ON 28 OCT 2004

L1 1 S US20020082433/PN  
SEL RN

FILE 'REGISTRY' ENTERED AT 13:43:37 ON 28 OCT 2004

L2 68 S E1-E68  
L3 63 S L2 AND C5-C6-C6-C6/ES  
L4 19 S L3 AND 2/O  
L5 1 S L4 AND C20H26O2  
E C20H26O2/MF  
L6 146 S E3 AND 4432.3.65/RID  
L7 146 S L6 AND 4/NR  
L8 2 S L7 AND 2 METHOXY  
L9 STR  
L10 0 S L9 CSS SAM  
L11 12 S L9 SAM  
L12 234 S L9 FUL  
SAV TEMP QAZI939/A L12  
L13 32 S L9 CSS FUL SUB=L12  
SAV TEMP L13 QAZI939A/A  
L14 12 S L2 AND L13  
L15 20 S L13 NOT L14  
L16 3 S L15 AND (C21H28O4 OR C21H28O2)

FILE 'HCAOLD' ENTERED AT 13:59:44 ON 28 OCT 2004

L17 0 S L14  
L18 2 S L16  
SEL AN  
EDIT E1-E2 /OR  
EDIT /AN /OREF

FILE 'HCAPLUS' ENTERED AT 14:00:47 ON 28 OCT 2004

L19 3 S E1-E2  
L20 2 S L19 NOT MAZUR ?/AU  
L21 6 S L14  
L22 11 S L16  
L23 15 S L20-L22  
L24 3 S L23 AND (AGOSTON G? OR SHAH J? OR HUNSUCKER K? OR PRIBLUDA V?  
L25 2 S L23 AND ENTREMED?/PA,CS  
L26 3 S L1,L24,L25  
L27 12 S L23 NOT L26

FILE 'USPATFULL, USPAT2' ENTERED AT 14:03:09 ON 28 OCT 2004

L28 4 S L14 OR L16

FILE 'REGISTRY' ENTERED AT 14:03:30 ON 28 OCT 2004

FILE 'HCAOLD' ENTERED AT 14:03:52 ON 28 OCT 2004

FILE 'HCAPLUS' ENTERED AT 14:05:22 ON 28 OCT 2004

L29 1 S L20 AND L21,L22  
L30 2 S L20,L29  
L31 10 S L27 NOT L30

FILE 'USPATFULL, USPAT2' ENTERED AT 14:07:42 ON 28 OCT 2004



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